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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) Abstract

The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.

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## DESCRIPTION

Human Proteins Having Hydrophobic  
Domains and DNAs Encoding These Proteins

## TECHNICAL FIELD

5 The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human  
10 cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to  
15 express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

## BACKGROUND ART

25 Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal  
30 manner such as the injection or the drip, so that there are

hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory  
5 proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is  
10 expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof  
15 include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-  
20 cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane  
25 proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,

the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

#### OBJECTS OF THE INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

#### BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.

Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.

Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.

Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.

Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.

Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.

Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.

Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.

Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.

Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.

Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.

Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.

Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.

Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.

Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.

Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.

Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.

Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.

Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.

Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.

Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.

Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.

Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.

Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.

Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.

Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

#### SUMMARY OF THE INVENTION

As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

#### DETAILED DESCRIPTION OF THE INVENTION

The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T<sub>7</sub>, T<sub>3</sub>, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region. 5  
Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system, and so on. 10

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pXal, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells, *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium phosphate method, the liposome method, the DEAE-dextran method, and so on. 20 25 30

After one of the proteins of the present invention is

expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on. 5 10

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the 15 20 25 30

11

scope of the present invention.

5 The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method by cDNA cloning, and so on.

10 The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)<sup>+</sup> RNAs extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as the primers for the RT-PCR method using an mRNA isolated from human cells.

30 The cDNAs of the present invention are characterized by

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6 comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and



131 to 150 shall come within the scope of the present invention.

In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

#### Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

5 levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. 10 proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products. 15

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987. 20

#### 25 Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be 30

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured. 5

#### Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1i65, HT2, CTLL2, TF-1, Mo7e and CMK. 20

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnoli et al., J. Immunol. 145:1706-1712, 1990; Bertagnoli et al., Cellular 25 30

Immunology 133:327-341, 1991; Bertagnoli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Krusbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon  $\gamma$ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; devries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6- Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.

6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Krusbeek, D.H. Margules, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as affecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, leishmania spp., malaria spp.

and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to induce immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or

tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and , microglobulin protein or an MHC class

II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7, Immunologic studies in Humans); Herrmann et al., 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann, et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J.

Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnoli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnoli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porcador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamal et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

#### Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complementary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Bridgell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooner, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### 25 Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is



not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

trauma and cerebrovascular diseases such as stroke. peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

6 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

10 It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

25 A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

30 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

5 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglestein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

#### Activin/Inhibin Activity

10 A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals.

15 Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., *Endocrinology* 91:562-572, 1972; Ling et al., *Nature* 321:779-782, 1986; Vale et al., *Nature* 321:776-779, 1986; Mason et al., *Nature* 318:659-663, 1985; Forage et al., *Proc. Natl. Acad. Sci. USA* 83:3091-3095, 1986.

#### Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J.E. Coligan, A.M. Krulsbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. *J. Clin. Invest.* 95:1370-1376, 1995; Lind et al. *APMIS* 103:140-146, 1995; Muller et al. *Eur. J. Immunol.* 25: 1744-1748; Gruber et al. *J. of Immunol.* 152:5860-5867, 1994; Johnston et al. *J. of Immunol.* 153: 1762-1768, 1994.

#### Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

#### Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Blier et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenberg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

#### Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

#### Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities: A

39

protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

#### Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors, or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

40

embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### Examples

The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

#### (1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

## (2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a T<sub>7</sub>T rabbit reticulocyte lysate kit (Promega). In this case, [<sup>35</sup>S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l of T<sub>7</sub>T rabbit reticulocyte lysate, 0.5  $\mu$ l of a buffer solution (attached to the kit), 2  $\mu$ l of an amino acid mixture (without methionine), 2  $\mu$ l of [<sup>35</sup>S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5  $\mu$ l of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

out by adding to this reaction system 2.5  $\mu$ l of a canine pancreas microsome fraction (Promega). To 3  $\mu$ l of the resulting reaction solution was added 2  $\mu$ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

## (3) Expression by COS7

*Escherichia coli* cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13KO7 (50  $\mu$ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with 1 x 10<sup>6</sup> COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the resulting cells was added a suspension of 1  $\mu$ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3  $\mu$ l of

TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed, the cell surface was washed with TDMM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the culture medium was replaced by a culture medium containing [<sup>35</sup>S]cysteine or [<sup>35</sup>S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

#### (4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (Genbank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

*elegans* hypothetical protein F45G2.c (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

Table 2

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10  HP  MAKYLAQITVGVGVGRAPARLRQEF-----AASRAADARGRGHRSAAASNL-
      . . . . .
15  CE  MPNRTALKVALAAGEVAKALTRAVERDEIKQOAAARHAASFGSASETRNANSNAK
      HP  GLSLQEAQOITLV- SKLSPEEVQKNVHELPKVNDKSVGSFYLGSKVNAKERLDEEL-K
      * . . . . .
      CE  GISLEESIQLTANVKPEINREVERKHELFNINDKSGGTLYLQSKVYRAKERLDEEFG
      HP  IQAQEDREKQMPHT
      * . . . . .
      CE  IELKEEKKEENAKTE

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02593> (SEQ ID Nos. 2, 12, and 22)

Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,

and a 198-bp 3'-untranslated region. The ORF codes for a protein consisting of 131 amino acid residues and there existed four putative transmembrane domains at the C-terminus. Figure 2 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to a human OB-R gene-related protein (EMBL Accession No. Y12670). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human OB-R gene-related protein (OB). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the entire region.

Table 3

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HP MAGIKALISLFGGAIGLAFIMLGCAPIYKNTWPLFVLFFYLSPICYIARRLVDDTD
    ***** * .***** . .***** . .***** . .***** . .***** .
OB MAGVRLVALSFGAIGLTFIMLGCALEDYGVWPLFVLIFHALSPDIPHIKRVTVDS
HP ANSNACKELAIFLTGIVWSAFGLPIVFARAHLEWGACALVLTGNTVIFATILGFLVF
    * .***** .***** .***** .***** .***** .***** .***** .
OB ATSSACRELAYFTTGIWVSAGFPVILARVAVIKWGACGLVLAGNAVIFLTIQGFLLIF
HP GSNDDFSWQW
    * .***** .
OB GRGDDFSWEQW

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10195> (SEQ ID Nos. 3, 13, and 23)

Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the



present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.5% in the entire region.

Table 4

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5  HP MAKHEQILVLDPTDLKFGPTDVVTNLKLNPSDRKVCVKITAPRKYCVRNSGI
    *****
10  AP MASHEQALILEPAGELRFGPTDVVTADLKLSNPTDRICFKVITAPRKYCVRNSGI
    HP IDGSTVTVSVMLQFPDYDPNEKSKHKMVGITFAPNTSD--MEAVKTEARPELDMSKL
    .....
15  AP LEPKTSIAVAVMLQFPNYDPNEKNKHKMVGADPHVESQELLMDADPESLMDTKL
    HP RCYFENRPNENDKLNDEPSK-----AVPLNASKODGPPKP--HVSILNDTE
    *****
    AP RCYFEMPDGSHQAPASDASRATDGAHRSSEALDPTVASRKTETQSPKRVGAVGASAGED
    HP TRIMAECKRIQGEWKLSEENRHLRDEGLRKRVAHSD--KPGSTSTASFRDNTSPPLP
    .....
20  AP VKLQHELKKAQSEITSLKGENSQLKDEGIRLKRKVAWTDVSPPLNPSAPAAVRAFP
    HP SLIVIAIAIFIGFLGKFTL
    ....*...*...*...*
    AP PIVYVVAAILIIGLIGKFTL

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25 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA447905) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10423> (SEQ ID Nos. 4, 14, and 24)

Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

15 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

25 Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

15 <HP10507> (SEQ ID Nos. 6, 16, and 26)

Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

16 <HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

30 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

30 The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen



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protein was similar to the *Xenopus laevis* cortical granule lectin (EMBL Accession No. X82626). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *X. laevis* cortical granule lectin (XL). Therein, the marks of '-', '+', and '.' represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the region other than the N-terminal region.

Table 6

15	HP MNGQSFLLFIATRGWSTDEANTYFKWPTCSSPSLPSRCKEIKDCEPSAFDGLYFLAT	*****	..***.
	..**		
	XL MLVHILLILLYTGLSGCEPVIVASKNWVKQLDCDFRSCKEIKDSNEAODGIYTLTS		
	HP PNGVITYQPCDMTSGGGGWTIVASVHENDRGRCTVGDNRSSQQGSKADYPRCDGNMANY		
	..*..*****	*****	*****
20	XL SDGISYQPCDMTNGGWTIVASVHNNMAGCTIGDRSSQQGNRADYPRCDGNMANY		
	HP NTFSASAPASDDYKMPGYDIOAKDLGIWHPNKSPMOHMNSSLIRYRTDTGFLQTLG		
	..*..*****	*****	*****
	XL NTFSASAGASDDYKMPGYDIEAIVNLGVHVPNKTPLSVWNNSSLQRYRTDGIILFKHG		
	HP HNLFGITYQKIPVKYGEKGCWTDNGPVPVYDFGDAQKTASYSYSPYGGREFAGFVQPRV		
	..*..*****	*****	*****
25	XL GNLFSLYRIYPVKYIGISCKSDGPVIVYDLSAKLTASFSPDRSQPFGYIQPRP		
	HP PNNRRANALCAGNRVTGCTNTEHCIGSGGYPFASPPQCCDFSGDWSGYCTHVGYSSS		
	..*..*****	*****	*****
	XL INTKAALALCPGKMESCNVENVCIGGGYFPEADPRQCGDPAADYFVGTKKFNAG		
	HP REITEAAVLLEFYR		
30	*****		
	XL IEITEAAVLLEFYL		

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R06009) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID Nos. 32, 42, and 52)

10 Determination of the whole base sequence of the cDNA insert of clone HP02515 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 176-bp 5'-untranslated region, a 690-bp ORF, and a 71-bp 3'-untranslated region. The ORF codes for a protein consisting of 229 amino acid residues and there existed a putative secretory signal at N-terminus and one putative transmembrane domain at the C-terminus. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 26,000 predicted from the ORF. In this case, the addition of a microscope led to the formation of a product of 25.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from phenylalanine at position 28.

30 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/ST2 receptor binding protein (GenBank Accession No. U41804). Table 7 shows the



the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.8% in the entire region.

Table 8

10 HP MHPQELPRLAFLULLLLLLLPBBC--PAHSATRPDPWESLBARQAPAFMDQAKGIEIT  
\*\*\*\*\*  
PC MMSRPAKRALLLLELGAABSVBARQPRARTPDMFSLDSRPLPAWDFEAKPGVIT  
HP HMGVSVBPFGSEMFNTYQKKEIKYUEFMNDVBPFSFKVEDPGLFTAKFPNANQMD  
\*\*\*\*\*  
PC HMGVSVBPANGESEMFNTMQSGRQYQAPFMDVBPFSVADBPQFTAPFHPREMD  
HP IYQASAKAYULTSKHNEFTLMGEYSMMNNAIDEGKRIUYELVALIRNTDLRFGIL  
\*\*\*\*\*  
PC LFOAGAKAVULTKTHNEFTWMPBPVSHMNNKSXDVEPHDLVGELETLAKR--NIRYGL  
HP YSLPEWEPRLPLEDESSFHKQRPVSKTLYELVELYNNQPEVMSDQDGAPOQYNN  
\*\*\*\*\*  
PC YHSLHEWPRYLILDKXNEFKQNHVSAKTPRELYDLVNSYKPYLINSDEMECPPTYNN  
HP STGFPLANTYNEBPVAGTVYTNRMAGASICKHNGUYTCSDBYNGHILPKHMCNCTIDK  
\*\*\*\*\*  
PC STNEFLMULYNDPVADEVVYNDRMNQNSCHHGGUYNCEDEKFXQSLPDKHMECTSIDX  
HP LSNGRTRREGISDIYETIEELVQYLETYSCGNLLMNIPTLDOETISVFEZELRQMSW  
\*\*\*\*\*  
PC PSNGRTRRMDALDVPEESITIELVQYSLSGNYLNIIGTPKQDLJVPRIQEBLAVGNK  
HP LKXNGALYETHTMSQNDTVPRDVWYISKRREKUYAIFLAKWTSQQLTGPRAKILDA  
\*\*\*\*\*  
PC LSNNGALYASKRPNQVQEKATTSWYIYSKGA--VYAFIHPWENOVNLSEPTT--ST  
HP TEVYKLGHGQPLMISLEONGIHWELPOLITHQPCCKGMYALATNYI  
\*\*\*\*\*  
PC TKTYMLGIGQDLKMSIDPCKGFIJSLPRLPBPAPBAEAMFTIKTLGXK

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. M28668) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

10 <HP10357> (SEQ ID Nos. 34, 44, and 54)

Determination of the whole base sequence of the cDNA insert of clone HP10357 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 113-bp 5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-untranslated region. The ORF codes for a protein consisting of 99 amino acid residues and there existed two putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 11 kDa that was almost identical with the molecular weight of 10,923 predicted from the ORF.

25 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA477156) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30  
<HP10447> (SEQ ID Nos. 35, 45, and 55)

### Determination of the whole base sequence of the cDNA

5 insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

10 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10477> (SEQ ID Nos. 36, 46, and 56)

20 Determination of the whole base sequence of the cDNA insert of clone HP10477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,884 predicted from the ORF.

The search of the protein data base using the amino

acid sequence of the present protein revealed that the protein was similar to the human peptidoglycan recognition protein (GenBank Accession No. AF076483). Table 9 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human peptidoglycan recognition protein (PG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.8% in the entire region.

Table 9

15	HP	MVDSLLAVTLNGLTLFLRGSTQSHPDLTGEGCDQLSAPRTTLLDPRASLTITKAFLL	
	HP	NGALDGVILGDTLSRTPEPSPSLSHLSQYVGAVRDPGERSNFRQNGAALTSASILA	
	HP	QQWGTILVILQRLPEVHLQLOCHSQEQLAQVAANATKEFTEAFICCPAIFRCRWGAAPY	*** ** *
	PG	MSRRSMLLAWALPSLLRLGAAQETEDPACCSPIVPRNEWKALA-	
20	HP	RGRPKLLQLPLGLFLYVHTYVPAPCTDTRCAANNRSMQRYHQDTQGWGIDIGYSFVYGS	.. * * * * * .. * * * * * .. * * * * * .. * * * * *
	PG	SECAQHLSLPLRVVVVSHY--AGSSCNTPASCCQQQARNVQHYHMKTLGWCVDVGNFLIGE	
	HP	DGTYEGRGHWVGAHTLGH-NSRGGVAIVGNVYTAALPTAAALTVRDTLPSCAVRAGL	** *
25	PG	DGLVYEGRGWFTGAHSGHLMNPMISIGISFMGNVHDRVFTFOAIRAAQGLL-ACGVAQGA	
	HP	LRPDYALLGHRLQVLTDCPDGALFDLLRTWPHFTATVPRPARSVSKRSRREPPPTLPA	***. *
	PG	LRSNVYLKGRDVRQTLSPGNQLYHLIQNWPHYRSP	

30 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration



of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10513> (SEQ ID Nos. 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

Table 10

HP	MGSPRGAGVVAAGLLGAGACYCIVRLTRGRRG
5	
10	KI RGRGRPVAMQKRPPEYDEILGVRDLKRVLLQKSDDPFIQVALLTSSNNANYSN HP DRELGINSSKSAEDLTGSDYDVLNAEQKLXLYLESFEDVYIERALITLGNNAFSSV * .....
15	KI QETIRKLGLPIIANMINKTDPHIKEKALMAANNLSENVENGRLQVYKXVMDIMASN HP NQAIIRRELGIPIVANKINHSQSIKEKALNALNLSVVENQIKYQVILKLLNLSEN * .....
20	KI LNSAVQVGLKFTNMTITNDYQHLVNSIANF--FRLLSGGGRKIKVELIKLSFAFN HP PAMTEGLRAQVDSFSLYDSHVAKELLRVLTLPQNIKNCIXGHILAVQPTPEGSL * .....
25	KI PDMLKRLSTQVPASFSLYNSVSESLINALTPEIYIDNIRAE--VENYREFPKGSL HP FFL-LNGEECAQKIRALVDHDAEYKENVYTIIPKI * .....
30	KI FYLCCTSGVCVKIRALNHHDLVKKVYIKLVNKF

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N92228) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10540> (SEQ ID Nos. 38, 48, and 58)

Determination of the whole base sequence of the cDNA insert of clone HP10540 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA420715) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10557> (SEQ ID Nos. 39, 49, and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.

consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

25	HP M-ASLLCCGPKLAACGVLSANGVIMLMIGIFPNVHSAVLIEDVPFTEKDFENGPNQIY
	*        ***    *    *    *    *    *    *    *    *    *    *    *
	CE MGKICPLMGPKMSAFNCWHSVWGVIETLLGVFFIQAATLFFDLHF-EGHGKVPSSVID
	HP NLYEQVSYNCFIAAGLYLLGGFSPCQVRLNKRKEYMVR
	*        *    *    *    *    *    *
30	CE AKYNEKATQCIWAAGLYAVTLIAVFWQ---NKYNTAQIF

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human progesterone binding protein (EMBL Accession No. A7002030). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human progesterone binding protein (PG). Therein, the marks of '-', '+', and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.5% in the C-terminal region of 151 amino acid residues.

Table 12

HP	PG	HP	PG
HP	PG	HP	PG
MAAGDGVKLTGSGSESSNDGSESPGDAGAAAGGMAAALALTTGGEMLNVAL	MAAGDGVKLTGSGSESSNDGSESPGDAGAAAGGMAAALALTTGGEMLNVAL	MAAGDGVKLTGSGSESSNDGSESPGDAGAAAGGMAAALALTTGGEMLNVAL	MAAGDGVKLTGSGSESSNDGSESPGDAGAAAGGMAAALALTTGGEMLNVAL
HP RRLRLPLAALALVLAAPGLPTARAGTPRPARCPPV--RLFTEELARYGGEEDQPI	HP RRLRLPLAALALVLAAPGLPTARAGTPRPARCPPV--RLFTEELARYGGEEDQPI	HP RRLRLPLAALALVLAAPGLPTARAGTPRPARCPPV--RLFTEELARYGGEEDQPI	HP RRLRLPLAALALVLAAPGLPTARAGTPRPARCPPV--RLFTEELARYGGEEDQPI
PG VALVLLGAYRLVMWNRGRLGAGAGGESPATSLPRMKRDFSLERQYDG-SRNPRI	PG VALVLLGAYRLVMWNRGRLGAGAGGESPATSLPRMKRDFSLERQYDG-SRNPRI	PG VALVLLGAYRLVMWNRGRLGAGAGGESPATSLPRMKRDFSLERQYDG-SRNPRI	PG VALVLLGAYRLVMWNRGRLGAGAGGESPATSLPRMKRDFSLERQYDG-SRNPRI
HP YLAIRGVVFDVTSKGKPYGRGAPYNALTKDSTRGVAKWSLDPAJLTHDTTGLTAKELA	HP YLAIRGVVFDVTSKGKPYGRGAPYNALTKDSTRGVAKWSLDPAJLTHDTTGLTAKELA	HP YLAIRGVVFDVTSKGKPYGRGAPYNALTKDSTRGVAKWSLDPAJLTHDTTGLTAKELA	HP YLAIRGVVFDVTSKGKPYGRGAPYNALTKDSTRGVAKWSLDPAJLTHDTTGLTAKELA
PG LLAVNGKVFDTGSKPYGRGAPYGFAGRDASRGLATFCLDKDALRDEYDLSDLNVAQ	PG LLAVNGKVFDTGSKPYGRGAPYGFAGRDASRGLATFCLDKDALRDEYDLSDLNVAQ	PG LLAVNGKVFDTGSKPYGRGAPYGFAGRDASRGLATFCLDKDALRDEYDLSDLNVAQ	PG LLAVNGKVFDTGSKPYGRGAPYGFAGRDASRGLATFCLDKDALRDEYDLSDLNVAQ
HP LDEV--FTKVKYKAKYPIYGYTARILNEDGSPNLDKPEDQPHDIKDER	HP LDEV--FTKVKYKAKYPIYGYTARILNEDGSPNLDKPEDQPHDIKDER	HP LDEV--FTKVKYKAKYPIYGYTARILNEDGSPNLDKPEDQPHDIKDER	HP LDEV--FTKVKYKAKYPIYGYTARILNEDGSPNLDKPEDQPHDIKDER
PG MESVREMEMQEKY---DIYG-RLLRGSEPS-EYTDDEEDTRDNHKKOD	PG MESVREMEMQEKY---DIYG-RLLRGSEPS-EYTDDEEDTRDNHKKOD	PG MESVREMEMQEKY---DIYG-RLLRGSEPS-EYTDDEEDTRDNHKKOD	PG MESVREMEMQEKY---DIYG-RLLRGSEPS-EYTDDEEDTRDNHKKOD

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA101709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (Genbank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of '-', '+', and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.

Table 13

HP MNPSTNLATGIPSKVKYSRLSSDGDGYDLOFKKTPKPIYKAIALATVWFLGAGFLI  
 AT MAYVDHAFSSDEDLMIQTGY-TVNRPVPUKEISLAVGLLVFGTGLGI  
 HP IIGSLLLSGYISKGGADRAVPVLIIGILVLPFGYHLRIAYTASGTYRGYSYDDIPDFDD  
 AT VLGFEMAYNRVG-CDRGHGIFIVLGGCLAFIPGIFYTRIAYYAYKGYKGFSEFSNIPSV

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA083574) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01467> (SEQ ID Nos. 61, 71, and 81)

Determination of the whole base sequence of the cDNA insert of clone HP01467 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 65-bp 5'-untranslated region, a 924-bp ORF, and a 447-bp 3'-untranslated region. The ORF codes for a protein consisting of 307 amino acid residues and there existed three putative transmembrane domains. Figure 21 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino

acid sequence of the present protein revealed that the protein was similar to the rat Sec22 homologue (GenBank Accession No. U42209). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat Sec22 homologue (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 94.6% in the N-terminal region of 241 amino acid residues. The protein of the present invention was longer by 53 amino acids at the C-terminus than the rat Sec22 homologue.

Table 14

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HP MSMLASVVRVDGLPLSASTDYEQSTGQECRYFMYMLSRKLAQLPDRCTLTKTHYNI
*****
RN MSMLASVVRVDGLPLSASTDCOSAGVQECRYFMYMLSRKLAQLPDRCTLTKTHYNI
*****
HP NFISLGVSYNMLCTENYPVLAFFSFLDELQKEFTTNNMKTNTAVRYPCEIEFDNFIQ
*****
RN NFISLGVSYNMLCTENYPVLAFFSFLDELQKEFTTNNMKTNTAVRYPCEIEFDNFIQ
*****
HP RTKORYNNPRSLSTKINLSDMQTEIKLRPPYQISMCELSGANGVTSFASVDCCKGACKLSS
*****
RN RTKORYNNPRSLSTKINLSDMQMEIKLRPPYQIOMCELSGANGVTSFASVDCCKGACKLSS
*****
HP AHORLEPATLSGIVGFILSLCCGALNLINGFHAIESLLQSDGDDPNYIIAFLFLGTAACLY
*****
RN AHORLEPATLSGIVAFILSLCCGALNLINGFHAIESLLQSDGEDFSYMIAFFLGTAACLY
*****
HP QCYLLVYTTGWRNVAKSFLLTGLICLCNNMVLVELRNLNOLFPHVITVGAFTVLQIWLURQAQG
*****
RN QMICLCLCGRKERT

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01956> (SEQ ID Nos. 62, 72, and 82)

Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (Sc). Therein, the marks of '-', '\*', and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 34.3% in the C-terminal region of 108 amino acid residues.

Table 15

5	HP	MTAGGLVANRRGRFMALELSGPGGSGRSDRGSGGDSLPVGYLDKQVPPTS
10	SC	MSGEPEYMAKHLDPYIEKNYIGNSNLPPSPPEGNSKGNVTRKQDATSQTSLA
	HP	VQETDRILVERKCDIALGPIKQIPMNLPIMWAGNTISIFPTMWCMAMRPIQALNAI
	SC	QKQITVLQVQKAMQMLQPAKSIPIPMIEMSYSGISLQIIPIMRLMILSPITAIYST
	HP	SATRK--MLESSQKFLQGLVYLIGNLGLALAV-Y-KGQSGLPETHASDVLARIEPE
	SC	RSARFPVLGNKATQSGVQTMFMIVTFQGLVMYIGYRKLNKSGILPNAKGDPLPNERIAH
	HP	RMEFSGGGLL
15	SC	YNNGLQWFSD

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAI59753) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02545> (SEQ ID Nos. 63, 73, and 83)

Determination of the whole base sequence of the cDNA insert of clone HP02545, obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 133-bp 5'-untranslated region, a 984-bp ORF, and a 636-bp 3'-untranslated region. The ORF codes for a



osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and therefore existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein (Genbank Accession No. U49611). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the both proteins were conserved.

Table 17

[illegible]

20 Furthermore, the search of the GenBank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, Accession No. AA317400) in ESTs, but, since they  
are partial sequences, it can not be judged whether or not  
25 any of these sequences codes for the same protein as the  
protein of the present invention.

<HP02631> (SEQ ID Nos. 65, 75, and 85)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,

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and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. A156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Caenorhabditis elegans hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

of the human protein of the present invention (HP) and the C. elegans hypothetical protein CELC2H12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.4% in the entire region.

Table 18

HP	MAWTKYQLFLAGLMLVTGSLNTLSAKWADFNPAEGCGSGKSHSFQHPFLQAVGMFLGFS
CE	KVAFVAVIISVMVVTGSLNTICAKWADSIKAD-----GVFFNHPFLQATCHFGEFL
HP	CLAAFYL-----LRCRAAGQSDS-----SVDPQQPFNPLFLPPALCDHGTSL
CE	CLVYFFLIFGKYKRYVNRANVGESGVTETSEKPTLPFPNPLFPFPALCDILGTSI
HP	MYVALNMTSASSFQMLRGAVIIFTGLFSAVPLGRRLVLSQMLGILATTAGLVVGLADLL
CE	MYICLNLTTRASSFQMLRGAVIIFTGLLSVGMNLNAQIKFKWGMFLVNLGLVIVGVTDIY
HP	SKHDSQHLKLESEVITGDLIIINAQIIIVAIQMLEEKVYKHNHPLRAVGTGLFGFVLS
CE	YDDPLDDRNATITGNLLIVHAQIIIVAIQMYEQKYLTKYDVPALFAVGLGLFGMVTLS
HP	LLVPMYIIPAG-SFSGNPRGTLEDALDAFCQVCGQPLIAVALLGNISSIAFFNFAGISV
CE	ILMIPFYIHVPRTFTNPEGRLEDVFIYANKEITEEPTIALALSGTVSVIAFFNFAGVSV
HP	TKELSATRRVLDSLTFTVIVWVLSALGWEAFHALQILGLFLLILIGTALYNGLRPLIGR
CE	TKELSATRRVLDSVRTLVIVWVSIPLFHEKFIQISGFAMLIIGTLIYNDIILIGPWR
HP	LSRGRPLAESEQRLLAGTRTPINDAS
CE	RNLLPNLSSHANCARCMLCICGGDSELIYEVEQDEHLNEA

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. M50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

Determination of the whole base sequence of the cDNA insert of clone HP10538 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF, and a 1911-bp 3'-untranslated region. The ORF codes for a protein consisting of 499 amino acid residues and there existed at least four putative transmembrane domains. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse pore-forming K<sup>+</sup> channel subunit (GenBank Accession No. AF056492). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse pore-forming K<sup>+</sup> channel subunit (MM). Therein, the marks of '-', '+', and '•' represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the N-terminal region of 241 amino acid residues.



which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA105822) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01470> (SEQ ID Nos. 91, 101, and 111)

Determination of the whole base sequence of the cDNA insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein 39.9 kDa (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire region.

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Table 20

HP MAPQNLSTFCILLLYLIGAVIAGDFYKILGVPRASIKDKKAYRKLALQLHFDNRNPD  
\* \* \* \* \*  
5 CE MRLNVSLLVASSLVAFCGRDFVKILGVAKNANANQIKKAYRKLAKELHFDNRQDD  
HP POAQEKQDLGAAVEVLSDEKSKQYDTYGEGL--KQGHQSSHGDI SFHFFGDFGMPG  
\* \* \* \* \*  
10 CE EMANEKFQDLSSAYEVLSDKEKRAYDRHGEAGVAKMGSGGGGHDFFSFFGDF-FG-G  
HP GTRQQRNIPRGSDIIVDLVLEEVYAGNFVVRNKPVARQAPGRKCNCEQEMRTT  
\* \* \* \* \*  
15 CE GGGHGGEGTPKADWTIDLFVLEEVYNGHFVLEIKRKAVYKQTSGRQNCHEHRT  
HP QLGEGRFQMTQVVEVCEPNVKNLNEERTEVEIEPGVDRGHEYPFICEGEPHVDGEPGD  
\* \* \* \* \*  
CE QMGQGRFQMFQVQVCEPNVKNLQENKLVLEVEVGADNGHQIIFHGECEPHIEGDPGD  
HP LRFRIVVVKHPIFERRGDDLYTNVTSLVESLVGFEMDITHLDGKHVHSRDKITRPGAK  
\* \* \* \* \*  
CE LKFKIRIQKHPRERKGDLYTNVTSIQDALNGFEMEIQHLDGHIUVQDRKVTWPGAR  
HP LMKKGELPNFNNNKSLIITFDVDPPEKQTEAREGIKQLLKQSSVQ-KVYNGLQC  
\* \* \* \* \*  
20 CE LRKKDGMPSELDNNKKHMLVTFDVEFPKTELSDEQAQIIEILQONTVPRAYNGL

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282838) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP002419> (SEQ ID Nos. 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.



Table 21

```

5  HP MKKVPATRTFRYSNCCLCCHVTRGTILLGWTYLIINAVVLLILLSALADPD---QY
      *****
KI MYSNSFKNNRSDRFYSTCCGCHVTRGTILLGWTYVWVLLMALITVEVTHPSNNAV
HP NFSSEELGDFEF-MDDANMCIALAISLMLICAMATGAYKORANMTIIFPCQIDF
      * . . . . . * . . . . . * . . . . . * . . . . . *
KI NIQEVIGNYYSSERMADNACVLEAVSLMTIISMLVGAISYQVGMIIFFCRLDEF
HP ALNMLVATVLIYFNSIOEYIRQLPPNPPYRDVMSVNPCLVLIILFISILFFKGYL
      * . . . . . * . . . . . * . . . . . * . . . . . *
KI VLSCIVAISSITVLPRIKEYLDQL-PDFPYKDDLALDSSCLLFIVLVEFALPIFKAYL
HP ISCVNRCYRIYNGNSSDVLVYVT-SNDTIVLLPPYDADFVNGANANPPPVASA
      * . . . . . * . . . . . * . . . . . * . . . . . *
KI INCVMNCKYIINNHNVEIAVYPAFAEPQVYLPYV-EMAVKMEKEPPPYLPA

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA173214) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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25 <HP02631> (SEQ ID Nos. 93, 103, and 113)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 588-bp ORF, and a 750-bp 3'-untranslated region. Although the 49th amino acid residue is encoded by a stop codon, it is likely that this codon encodes selenocysteine from the molecular weight

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of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsome led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

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The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cysteine was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

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Table 23

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5  HP MNHLLIMLLVLCALLLLVQLRFLRADGDTLMAENQGRPEWELTDVWVWVTGASS
    HP GIGELAYQLSKLGSLVLSARRVHELKRCLENGNLKEDLVLPDLDTGSHEA
    ****.*****.***.
    RN VKRSLKNGNLKEDLVLPDLADTSSHDI
    HP ATKAVLQEPGRIDILVNNGMSQSRSLCMQTSIDVTRKLIENLYGTVSLTKCVLPHMER
    10  ***.*****.***.***.***.***.*****.***.***
    RN ATKVTLQEPGRIDILVNNGVAHASIVENTNDIFKVLIEVNYLGTVSLTKCVLPHMER
    HP KQGRIVTVNSILGIISVPLISIGYCAKHALRGFNGRLTSLATYFGIIVSNICGPPVQSN
    *****
    RN NQGRIVVMKS

```

16 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T84331) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10031> (SEQ ID Nos. 95, 105, and 115)

Determination of the whole base sequence of the cDNA insert of clone HP10031 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF, and a 649-bp 3'-untranslated region. The ORF codes for a protein consisting of 487 amino acid residues and there existed eleven putative transmembrane domains. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

6 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELK07H8 (GenBank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELK07H8 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.



human protein of the present invention (HP) and the A. thaliana hypothetical protein IG002N01 (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 27.0% in the N-terminal region of 355 amino acid residues.

Table 25

HP	MTLFLNLML
5	AT MEITSPQSPSSNDVSVSVLSVNSMARRRSSAELSRNDGYESLCQVYQODSDR HP ALACSPVHTTSLKSDAKAASKTLEKSPSDKRVQDRGLVVDLKRESVYLEHRSYCSA .....*
10	AT LITFIVFFIVIPAVSIIVKVFADNVIOTESSIRQKGIKTDINQELITEHSK--AS HP KADRRHFAQDVIGVTPNNSHGVDVTVFGSKTQISPVNLQ-LKRRGRMEFEVTGLHDV .....*
15	AT ENSTRHYDYPVLAITP--CQSGSL--VLEGR-HNADKGMIOELRSKGNLSASKGLPKL HP DQGMRAVAKKAKGLHIVPRLLFEDWTYDPRNVLDSEDEIEELSKTVQVAKKQNHDF .....*
20	AT ---YNSCIFALKRMNFFTELVNFTYLVIMEALNS-REMEYNGIVLESMSRHAAYGVL HP VVEVNNQLSQKRVGLIMLTALBALHQAALLVIPALITPGTDQNGFTHEKEEQL .....*
25	AT HBDLARKALKFVKQLGDALHSTSSPRNNQHMOPMYVVGPPRSEKLOMTDPGEDIQFL HP APVLDSFSIMTYDVSTAHQPGNNAPLSWRACVQ-VLDPRSK---WRSKILLGLNFGM *****
30	AT KDSVDGFSIMTYDPSNPQPGNNAPVKNIDLTTLKLLGSSNNIDSNIAKRVLLGINFGN HP DVATSKDAREPVGARYIQTLKDRPRWVWDSQASEHFEYKKSRSRGHVVFPYTLKSLQ *****
35	AT DFTVSGGGGATGRDYLLALQKHKPTFRMDKESGEHLFWRODKNIKRAVFPYTLMSIL HP VRLLEARELGVSIMELGGGLDYFDLL *****
40	AT IRLNARLWIGIGISIMEIGDKGHFGKYAEASLEASSIFSGHPTDMQFRTPNROLSHNGS .....*

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

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protein of the present invention.

<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA insert of clone HP10541 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 7-bp 5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-untranslated region. The ORF codes for a protein consisting of 196 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 37 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 21,553 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 20 kDa from which the secretory signal is considered to have been cleaved and a product of 23 kDa which is considered to have a sugar chain being attached. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 41. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Leu-Thr at position 185).

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human zymogen membrane protein (GenBank Accession No. AF056492). Table 26 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human zymogen membrane protein (2M). Therein, the marks of -, \*, and . represent a

gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the C-terminal region of 133 amino acid residues.

Table 26

10	HP	MRVPGTTRPVTGSPCHRPENMLLLLTLLGGFTWAGKMYGPGGKGYFS-TTEDYD	..*****
20	2M	MLTVALLALCASAGNAIQARSSYSGEYSGSGGKRFSHSGNQILD	
30	HP	HBITGLRVSGLLLVKSVQKLGSDWDVKGALGGNTQEVTLQPGYITKVPVAFQAFLR	..*****
40	2M	GPITALRVRVNTYYIVGLQVRYGKVDYVGGANGDLEIFLHPGESVIQVSGKVKYLYK	..*****
50	HP	GMVWTSKDRYFYFGKLDGQISSAYPSQEGQVLGVYGVQVLLGIKISIGFEWN-YPLEEP	..*****
60	2M	KLVFVTDKRYLSFGKDSGTSFNAVPLHPNTVLRFISGRSGSL-IDAIGLHWDVYPTSCS	..*****
70	HP	TTEPVPNLTYSANSPVGR	

20 2M RC

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10550> (SEQ ID Nos. 98, 108, and 118)

Determination of the whole base sequence of the cDNA



Insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10590> (SEQ ID Nos. 99, 109, and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10591> (SEQ ID Nos. 100, 110, and 120)

Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA insert of clone HP01462 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF, and a 477-bp 3'-untranslated region. The ORF codes for a protein consisting of 483 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 41 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 72 kDa that was larger than the molecular weight of 55,838 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 21.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein ZK1058.4 (EMBL Accession No. Z35604). Table 27 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein ZK1058.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.6% in the entire region.

Table 27

	HP	MRAFTFCVLLVFGSVSEAKFDDFEDEEDIVEYDDNDFAEFEDVMEDSVTESPQRIIT	
5	CE	EDDE-DETVVELEGQENQEGDFEDADTQEGTSEFPYDDEEPEGYEDKP-----D	
	HP	EDDE-DETVVELEGQENQEGDFEDADTQEGTSEFPYDDEEPEGYEDKP-----D	
	CE	DDNEFAEFDEFGSSATQAEIQREGEPPVLKQKODFEEDFCGVVEEPEEAEKKEAD	
	HP	TSSSKNKDPITIVDPAPHLQNSWESYYLEILMTGLLAYIMNYIIGKNKNSRLAQAFNT	
10		.....	
	CE	SDAAPAPLKFADVPFAHFRSNWASYQVEGIVLVLIIILYINLYIGKTTWASTAQIFDM	
	HP	HRELLESFTLVGDDGTNKEATSTGKLNQNEHIYNLWCSGRVCCGMLLQLFLKQDL	
	CE	CRPTLEQFVAVVGDDGTTDLKMHPSLKHDTSTFSACVGRVNVNSLFLQMKRVKQDV	
15	HP	LNVLARMRPVSDQVQIKVTNN-DEDMTVYFVAGTRKALVRLQKEMQDLSEFCSDPKS	
	CE	VSRIHMTTPSGDKMTKASLETNTDPLIFAVGKKIASKYFKEMLDLNSFASERKQA	
	HP	GAKYGLPDSLALSEMGVTDGMDTRMWHFLTHYADKIESVHFSQFSGPKINQEGQP	
20		.....	
	CE	AQQNLPAWQVYADQNEVWFVSIIDPGVWSLLKKHDEAIEFIHISQFTGPKFAEGESYT	
	HP	LKLPDTKRTLLFTFNVPGSGNTYPKMEALLPLANNMVIYSIDKAKFRNLNREGKQADKN	
	CE	RLPEAQRYMFWSLNQLVGLG----QDEESVMEILNLVYLIDKARKHKLKDKAKVKAERR	
	HP	RARVEENFLKLTHTVQREAAQSRREKKRAEKERIMNEEDPEKQRLAEAAARREOKLE	
25		.....	
	CE	RKEFEDAFKQTHQFQEAQAARREKTRERKQKLMDSDPERKRLKREAKA--	
	HP	KKQMKKQLKVKAM	
	CE	-KSPMKKQLKVK	
30			

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02485> (SEQ ID Nos. 122, 132, and 142)

Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Caenorhabditis elegans hypothetical protein W01A11.2 (Genbank Accession No. U64852). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C. elegans hypothetical protein W01A11.2 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

Table 28

HP	MYEAPLPMPWRRLQTLAVLQVPSFLALETCT-V
5	.....*
CE	MLRLSSISGKNTLPDKICSSVSRLAPLVPMKRLLETAVGFIEMVILIMDLW
HP	GPYALLFTFRFWLLTVLYAAMWYLDKDKRGGGRHIOALRCWTIKYKDYPPISLVKTAE
10	.....*
CE	PFWLFTFMWFLVPLVAVWFYDPTPKASRRNNARAVANKYASYPPLNLITAD
HP	LDPSRNYIAGFBHGVLAAGAPANLCTESTGFSIFPGIRPHIMLTLMPRAPPPDYIM
15	.....*
CE	LPADRNYIIGSHGMEVSGFTAMSTNATGFEKPGIKSHIMTLNGQFYFPFRREGI
HP	SAGLVTSKESNAHILNRKGGNLIIGVGNQELDARPGSPYLLRNKGFRLATF
20	.....*
CE	MLGIEVSKESLEVTLCGKGRACAIVTGSASBALAHPMKNLTLINRGPCYALKF
HP	GAPLVPIFSFGENDLPDQIPNSGSLNLYIQNRLOKIMGISLPFHGRGVF-QYSFGLIP
25	.....*
CE	GADLVPMYNGENDLYEQYENPKGSRLEVOEKIKDFGLCPPLLRGSLFNQYLIGLP
HP	YRRPITTVGKPIEVOKTLHPSEEVNQLHORIKELCNLFPAHKLNFNPAQHLEFC
30	.....*
CE	FRKPVTVVNGRPIRVLTQDEPVEQIDELHAKYCDALYNLFEEYKHLHSIPDTHLIFQ

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D25664) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02798> (SEQ ID Nos. 123, 133, and 143)

Determination of the whole base sequence of the cDNA

insert of clone HP02798 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 31-bp 5'-untranslated region, a 804-bp ORF, and a 301-bp 3'-untranslated region. The ORF codes for a protein consisting of 267 amino acid residues and there existed four putative transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 30,778 predicted from the ORF. When expressed in COS7 cells, an expression product of about 26 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human DHHC-containing cysteine-rich protein (GenBank Accession No. U90653). Table 29 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human DHHC-containing cysteine-rich protein (DH). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the intermediate region of 100 amino acid residues. The positions of seven cysteines were conserved between the two proteins. The protein of the present invention also had the DHHC (Asp-His-His-Cys) sequence.

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Table 29

HP	MAPWALLSPGVLYRTGHTVLTWGI
5	DH MYKNNICNKPSTAPEKSVTAPQSPGSPPELQGRSRRNGSWPPEPLQIVANLLYL HP TLVTLFLHDTELQWEEQEGELLPLTLLVLLVLSLLYLAVALNDPCGVNVQPP-QEELK * * * * *
10	DH FFAVIGFGILVPLPHHWVPAGYACMGATPAGHLVVLTAVIDPADDNVRDYSYAGPLP HP EEQTAMVPPAIPLRRCRYCLVQLPLRHRHCRRCRRYRDHHCPCWENCVGERNIPLFV * * * * * DH IFNRSQAHNVIEDLHNCNLNVDSARSKHCSACNKCVCDFDHCKWLNVCVGERNVRLEPL HP VYLALQLVLLMGLYLAWSGLRFFQFWGLWLRSSGLLFATFELLLSLFLSLVASLLLVSHLY * * * * *
15	DH HVSASALLGVLLLVGLGGHICLRGVLCPHASAHQPTL

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D79050) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10041> (SEQ ID Nos. 124, 134, and 144)  
Determination of the whole base sequence of the cDNA  
Insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts

107

the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

```

HP MSTNNNSDPRRPNKVLRYKP---PPECCNDALDDPPEDYNNLGMIFSMCGMLKTKWCA
      ***** ..... ** *.....*****
CE  MOONGDPRTNRIVRYKPLDSTANQQAISDDPLPEYNNVLGMIFSMCGMLIRNKWCS
HP  WVAAYCSFISFANRSSEDTKQWMSFMLSISAVVMSYLGNDPQMPWTPPW
      *.....*.....*****
CE  WLAIVCSGISFANRTSDAKQIVSFMLSVSAVVMSYLGNDPSPPIIPWVTLIQS

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Furthermore, the search of the GenBank using the base

108

sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10246> (SEQ ID Nos. 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

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of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

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Table 31

```

HP MTLFHFNCFPALAYFPYFITYKSGLSSEYNFKNVCQAGVTYLFVQLCKMLFLATFFPTW
*****
TM MTLFHFNCFPALAYFPYFITYKCTDLSEYNFKNVCQAGVTYLFVQLCKMLFLATFFPTW
HP EGGYDFIGFEMKASVDVADLIGLNLVMSRNAGKEIKIMVAALGWATAELINSRCIPLW
*****
TM EGGYDFIGFEMKASVDVADLIGLNLVMSRNAGKEIKIMVAALGWATAELINSRCIPLW
HP VGARGIEFDWKYIQMSIDNSISLVHYIVASQVWMITRYDLYHTFRPAVLLMLFLSVYKA
*****
TM VGARGIEFDWKYIQMSIDNSISLGPYIVASQVWMITRYDLYHTFRPAVLLMLFLRVYKA
HP FMVETFVHLCSLGSMAALLARAVVTGLLALSTALYVAVVNVHS
*****
TM FMVETFVHLCSLGSMAVLMAGVVVVKGLLVIRNLAMYVAVVNVHS

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10392> (SEQ ID Nos. 126, 136, and 146)

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

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consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

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<HP10489> (SEQ ID Nos. 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

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Figure 47 depicts the

111

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10519> (SEQ ID Nos. 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

112

of the present invention.

<HP10531> (SEQ ID Nos. 129, 139, and 149)

Determination of the whole base sequence of the cDNA insert of clone HP10531 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF, and a 1092-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed five putative transmembrane domains. Figure 49 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R50695) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10574> (SEQ ID Nos. 130, 140, and 150)

Determination of the whole base sequence of the cDNA insert of clone HP10574 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 210-bp 5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-untranslated region. The ORF codes for a protein consisting of 428 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 50 depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the D. melanogaster GOLIATH protein (DM). Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of the 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the D. melanogaster GOLIATH protein.

Table 32

5	HP MGPPPGAGVSCGGCGGFSRLWCELLALSPQAGSRGAEAVWTAYLNVSVRVPHTGVNR HP TVWELSEGVQODSPLEFVAGVLVPPDGPGLNACNPHNTPTVTWGSIVQVSWLALI HP QRGCGCTFADKINHLAYERGASGAVIFNPGTENEVIPHSHPGAVDIIAIMIGNLKGTKIL DM MLEKWKQIKGKTRNIAAVITYQNIQDLS HP QSIQRGIQVTWIEVGKK---HGPWNHYISIFFVSFFIITAATVGYFIYSARLRNA DM LTLDKYNVTISIIEGRGVNTISSLNRTSVLFVVIS-FIV-DDILCWLIIFYIYQRYM HP RAQSRQRQKADAKKAIGRLQLRLKQDKEIGDGDSCAVCIELKPNDLVRLITCNH DM QAKDQOSRNLCSVTKKAIKNIPTTKGRFSD-EKOLDSDCCCAICIEAVKPTDTIRILPKH HP IFHKTCVDPWLEHRTCPMKCKDILKALGIEVDVEDGVSQVLPVSNISNSASSHEEDN DM EPHKNCIDPWLIEHRTCPMKCLDLVLFYGVVGDQIYQTPSPQHTAPIASIEEVPVIVVA HP RSETASSGYASVQGTDEPPELEHVQSTNESLQVNHNEANSVAVDVIPHDVNPFTFEDETP DM VPHGPQPLQFLOANSNNSFAPSHYFQSSRSPSSSVQOQLAPLTYOPHPQQAASERGRNS HP NQETAVREIKS DM APATPHAITASHQVTDV
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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAL55685) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

## INDUSTRIAL APPLICABILITY



The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, *Trends Pharmacol. Sci.* 15(7): 250-254; Lavarosky et al., 1997, *Biochem. Mol. Med.* 62(1): 11-22; and Hampel, 1998, *Prog. Nucleic Acid Res. Mol. Biol.* 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% more preferably at least 50%, and most preferably at least 75% of the length of a disclosed protein and have at least 60% sequence identity (more

preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table 33 below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 33

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) <sup>f</sup>	Hybridization Temperature and Buffer <sup>g</sup>	Wash Temperature and Buffer <sup>h</sup>
A	DNA : DNA	≥50	65°C; 1×SSC -or- 42°C; 1×SSC, 50% formamide	65°C; 0.3×SSC
B	DNA : DNA	<50	T <sub>h</sub> <sup>+</sup> ; 1×SSC	T <sub>h</sub> <sup>+</sup> ; 1×SSC
C	DNA : RNA	≥50	67°C; 1×SSC -or- 45°C; 1×SSC, 50% formamide	67°C; 0.3×SSC
D	DNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 1×SSC	T <sub>h</sub> <sup>+</sup> ; 1×SSC
E	RNA : RNA	≥50	70°C; 1×SSC -or- 60°C; 1×SSC, 50% formamide	70°C; 0.3×SSC
F	RNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 1×SSC	T <sub>h</sub> <sup>+</sup> ; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or- 42°C; 4×SSC, 50% formamide	65°C; 1×SSC
H	DNA : DNA	<50	T <sub>h</sub> <sup>+</sup> ; 4×SSC	T <sub>h</sub> <sup>+</sup> ; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or- 45°C; 4×SSC, 50% formamide	67°C; 1×SSC
J	DNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 4×SSC	T <sub>h</sub> <sup>+</sup> ; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or- 60°C; 4×SSC, 50% formamide	67°C; 1×SSC
L	RNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 2×SSC	T <sub>h</sub> <sup>+</sup> ; 2×SSC
M	DNA : DNA	≥50	60°C; 4×SSC -or- 40°C; 6×SSC, 50% formamide	60°C; 2×SSC
N	DNA : DNA	<50	T <sub>h</sub> <sup>+</sup> ; 6×SSC	T <sub>h</sub> <sup>+</sup> ; 6×SSC
O	DNA : RNA	≥50	55°C; 4×SSC -or- 42°C; 6×SSC, 50% formamide	55°C; 2×SSC
P	DNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 6×SSC	T <sub>h</sub> <sup>+</sup> ; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or- 45°C; 6×SSC, 50% formamide	60°C; 2×SSC
R	RNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 4×SSC	T <sub>h</sub> <sup>+</sup> ; 4×SSC

<sup>f</sup>: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

<sup>g</sup>: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

<sup>h</sup>T<sub>h</sub> - T<sub>h</sub>: The hybridization temperature for hybrids anticipated to be less than

50 base pairs in length should be 5-10°C less than the melting temperature ( $T_m$ ) of the hybrid, where  $T_m$  is determined according to the following equations. For hybrids less than 18 base pairs in length,  $T_m(°C) = 2(\# \text{ of A + T bases}) + 4(\# \text{ of G + C bases})$ . For hybrids between 18 and 49 base pairs in length,  $T_m(°C) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{ G+C}) - (600/N)$ , where N is the number of bases in the hybrid, and  $[\text{Na}^+]$  is the concentration of sodium ions in the hybridization buffer ( $[\text{Na}^+]$  for 1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

# CLAIMS

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.
2. An isolated DNA coding for the protein according to Claim 1.
3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.
4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.
5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.
6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1:

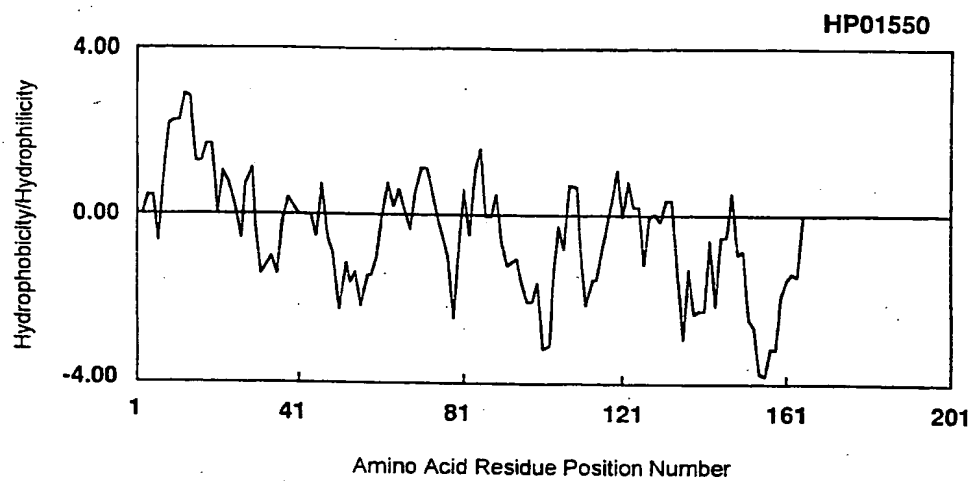


Fig. 1

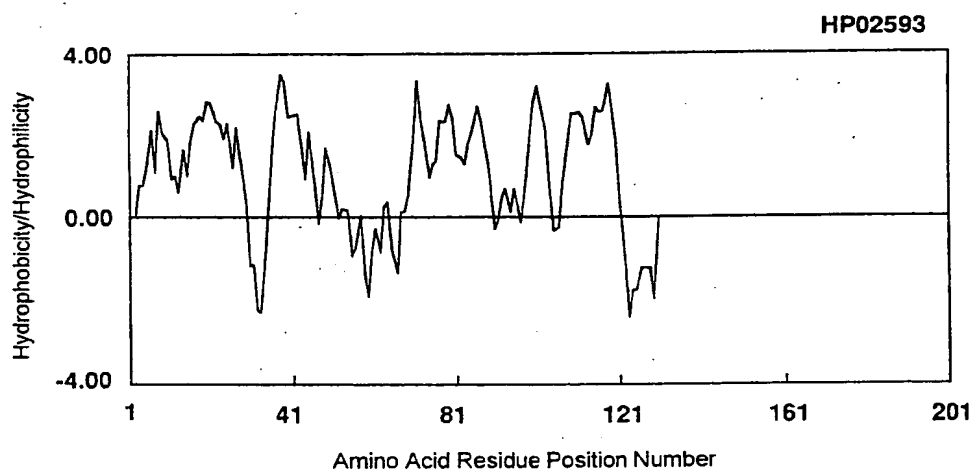


Fig. 2

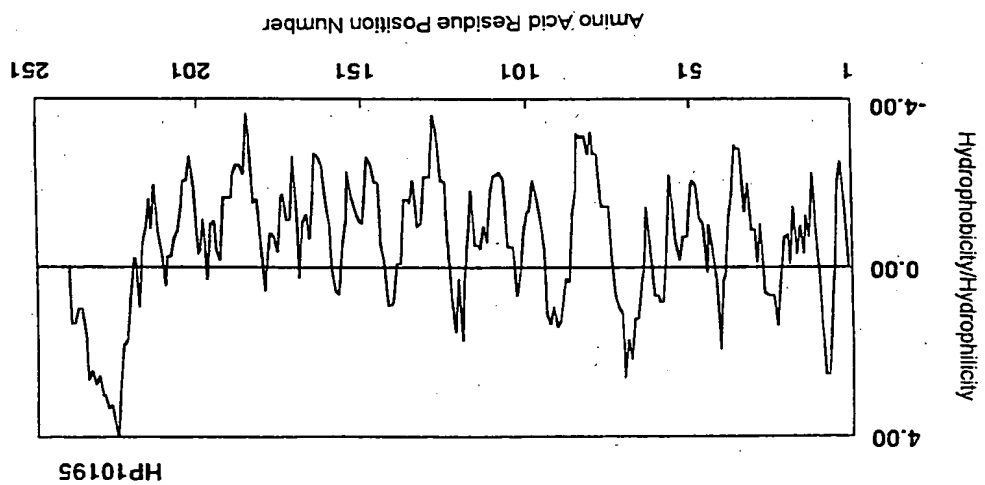


Fig. 3

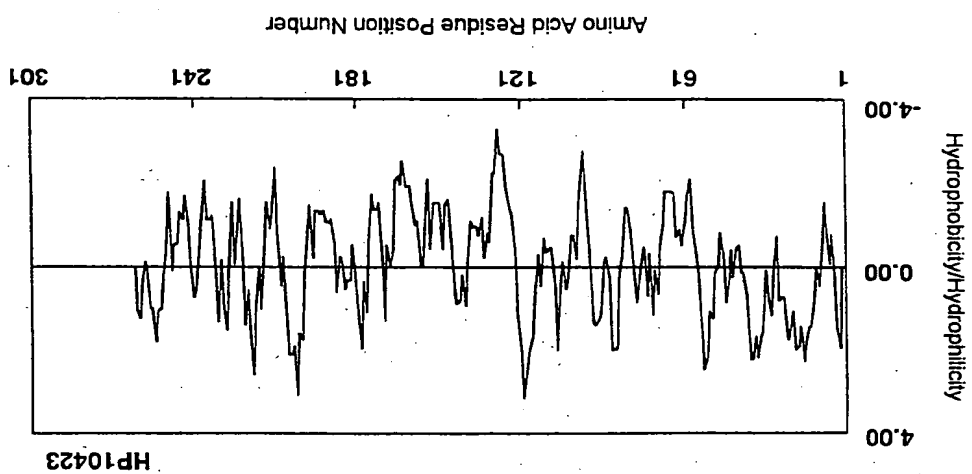


Fig. 4

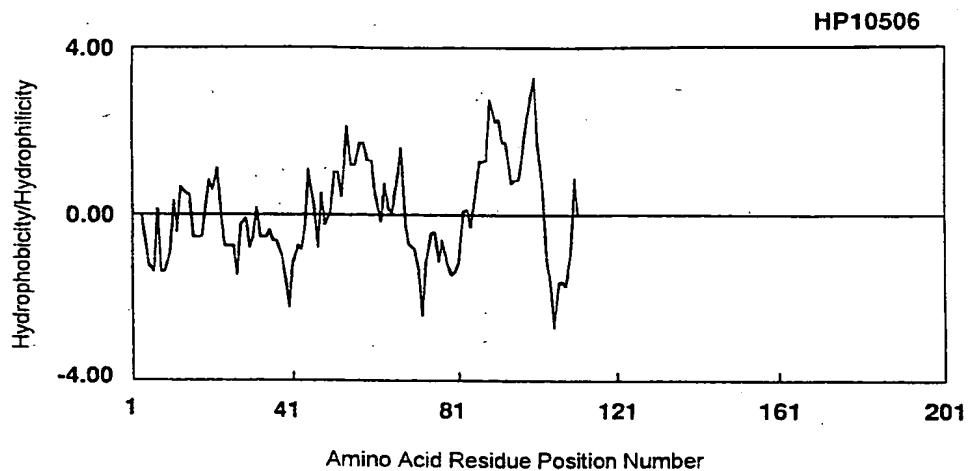


Fig. 5

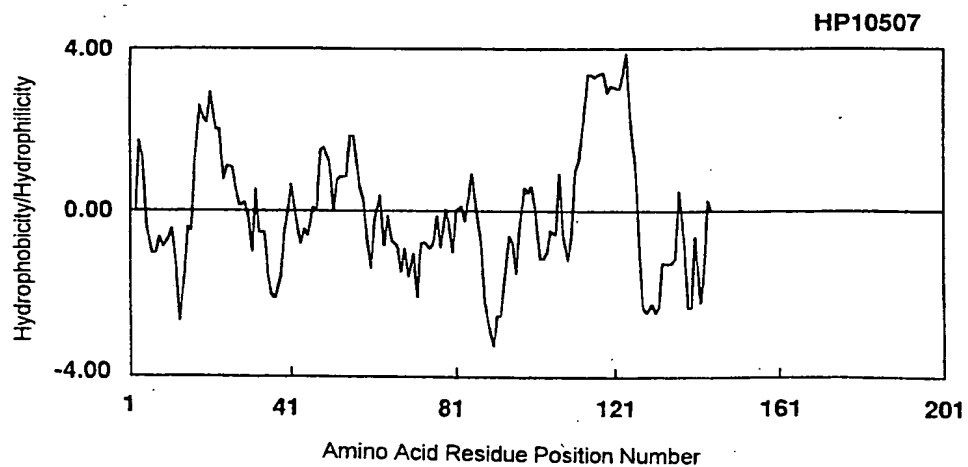
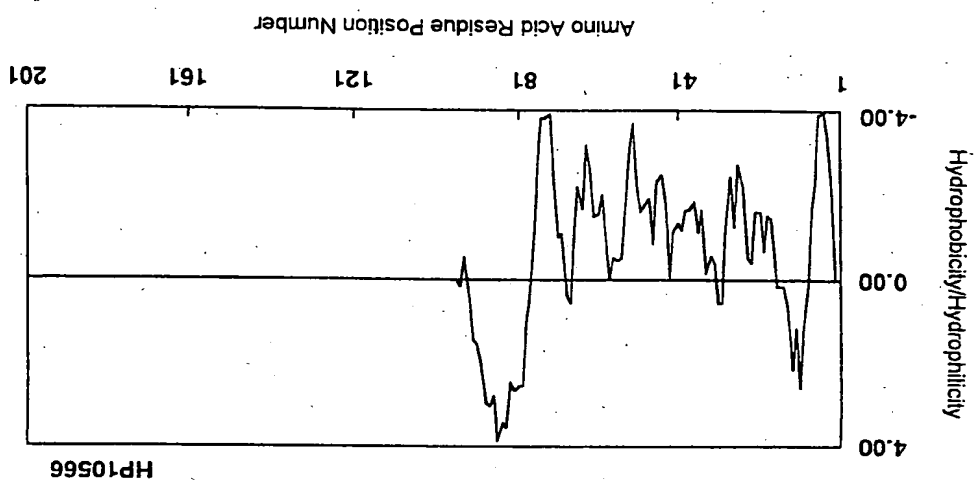


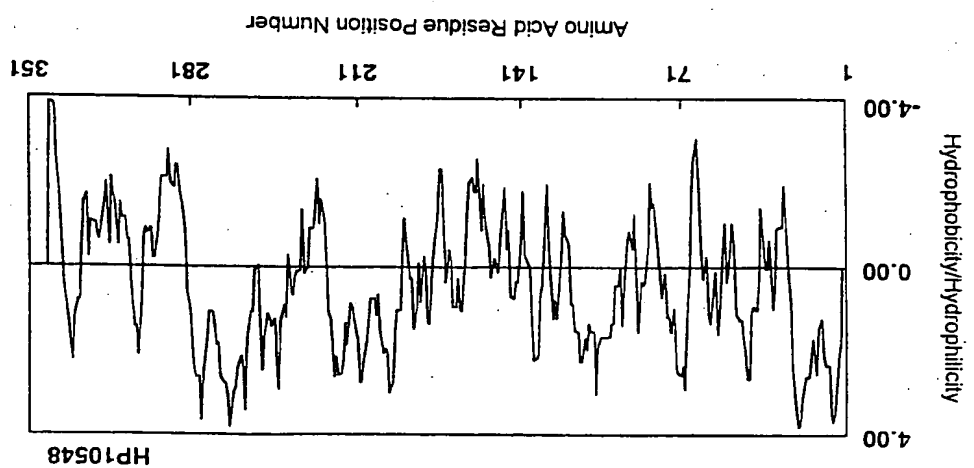
Fig. 6

Fig. 8



8/50

Fig. 7



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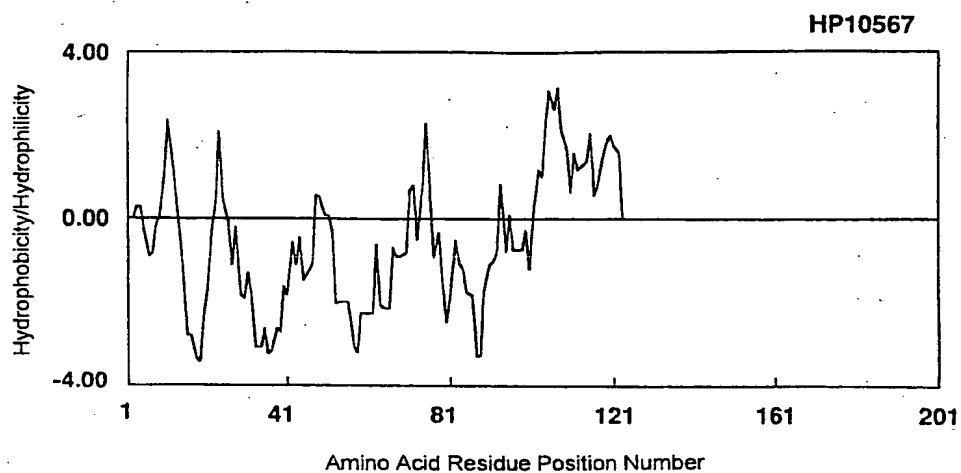


Fig. 9

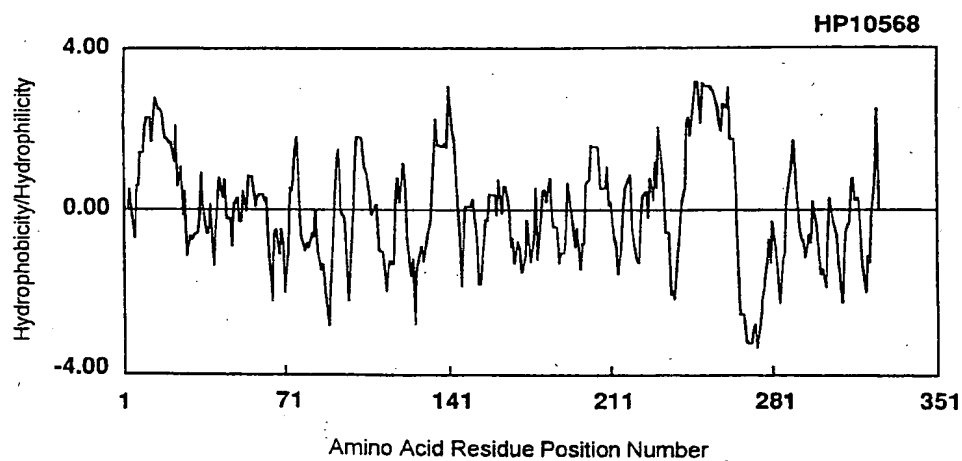


Fig. 10

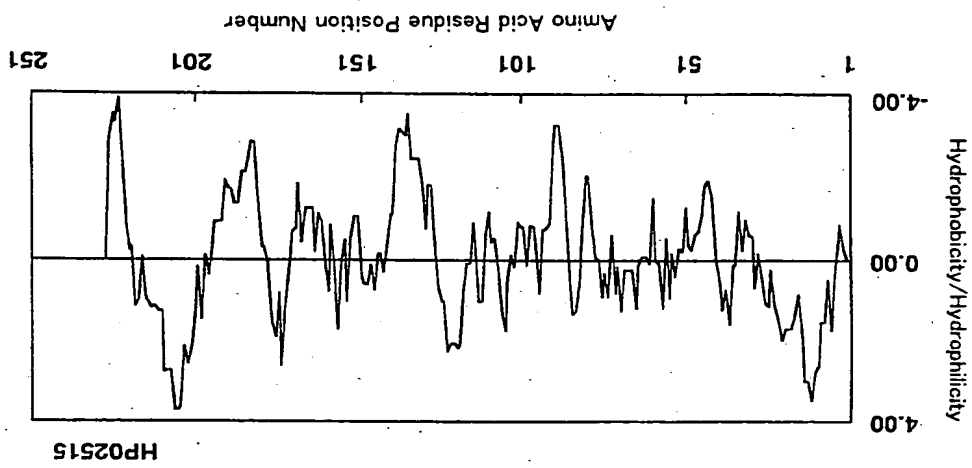


Fig. 12

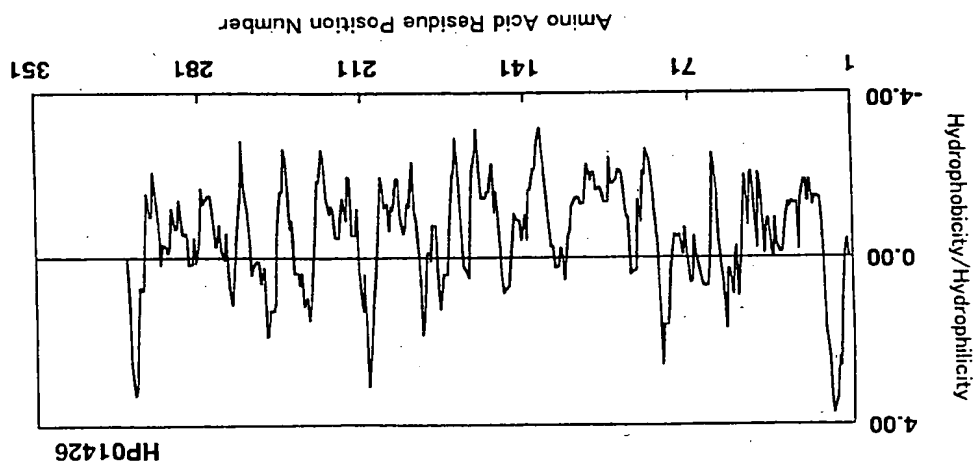


Fig. 11

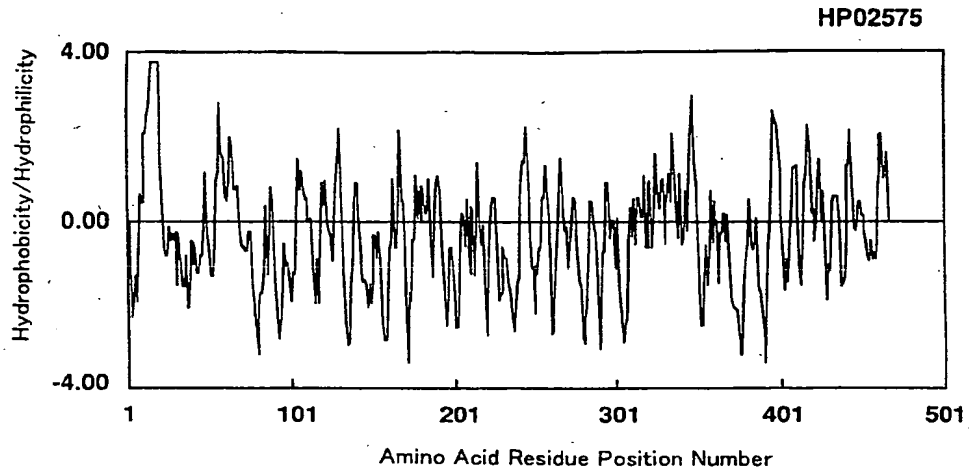


Fig. 13

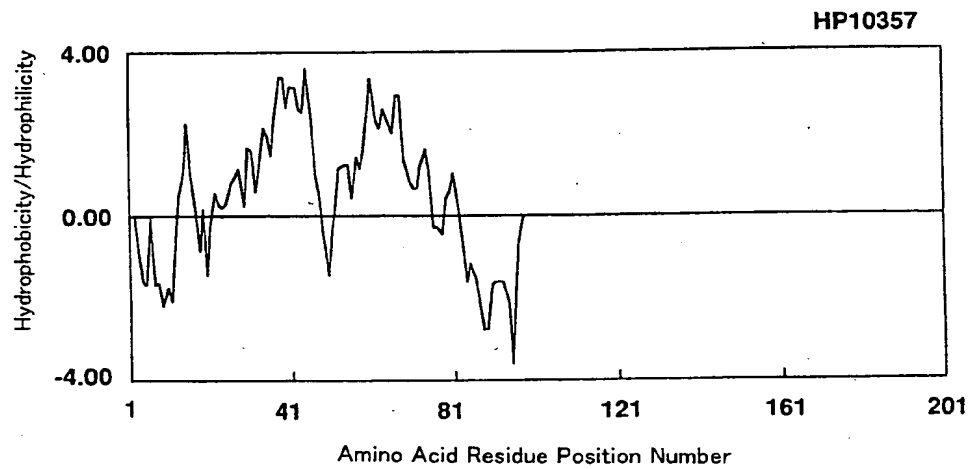


Fig. 14

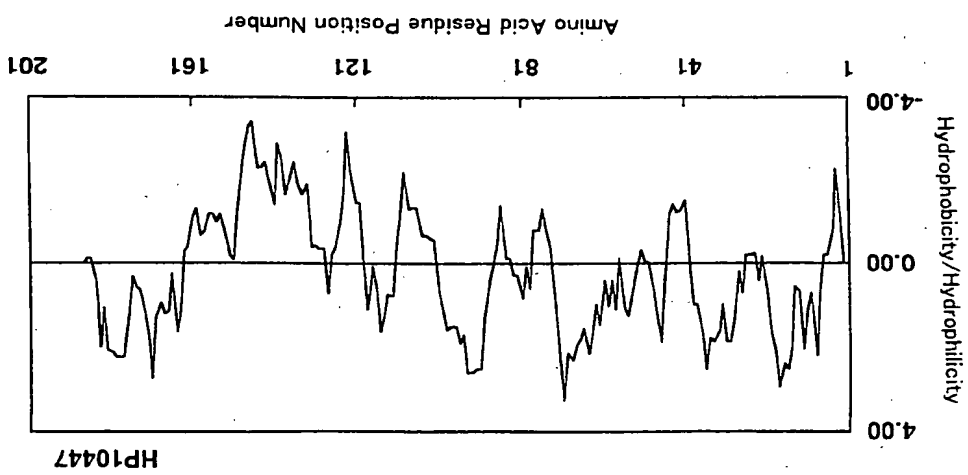


Fig. 15

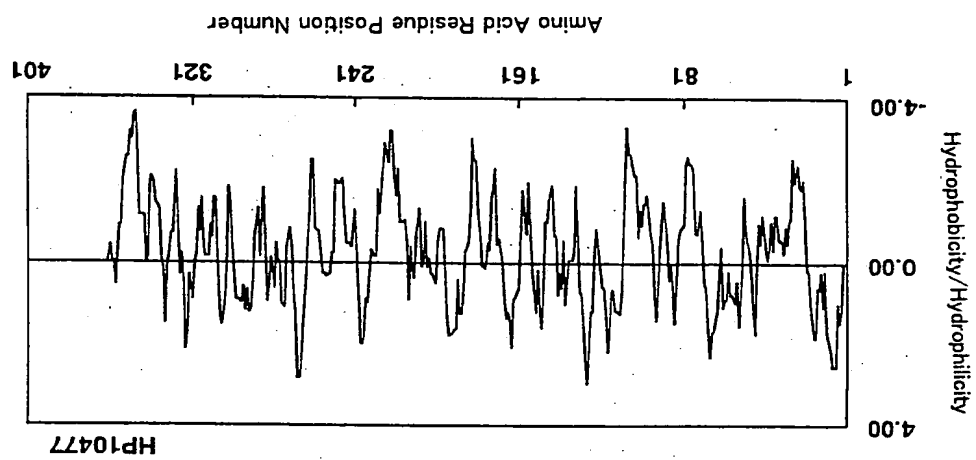


Fig. 16

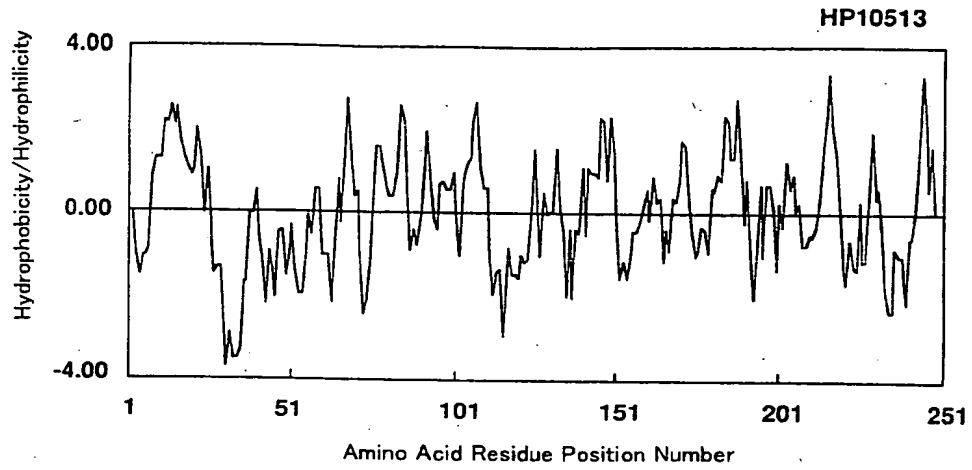


Fig.17

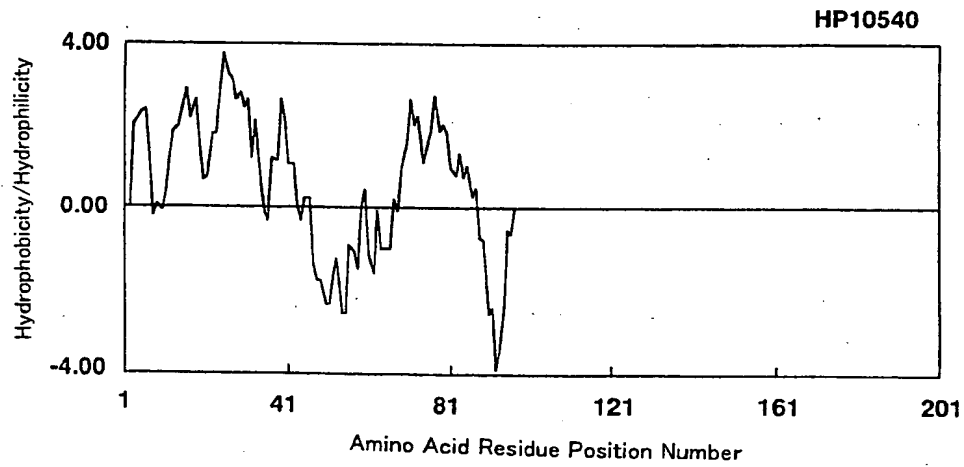


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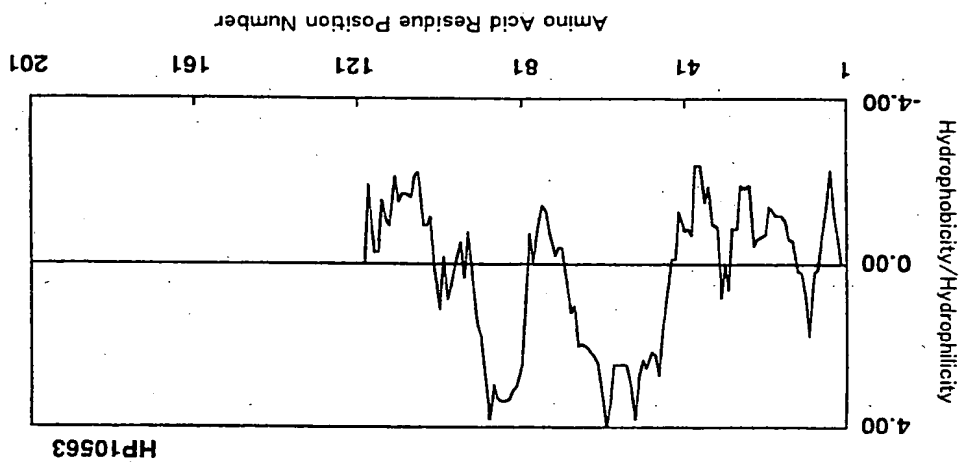


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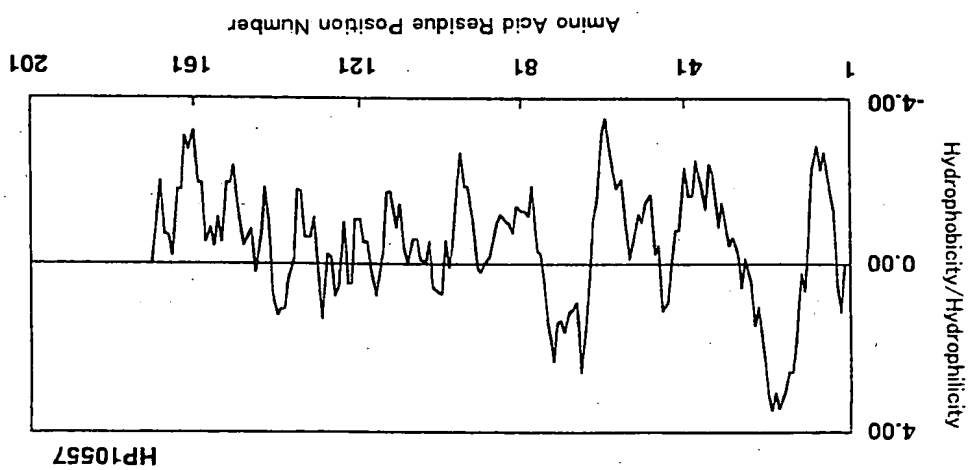


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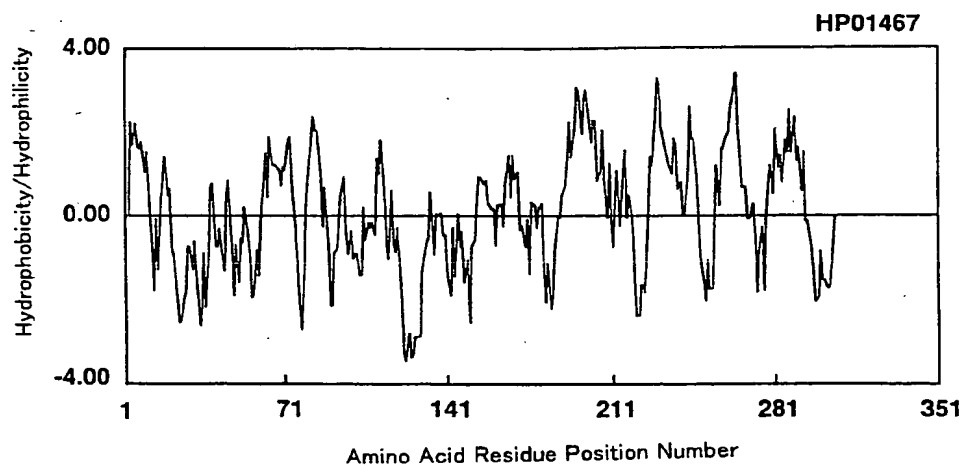


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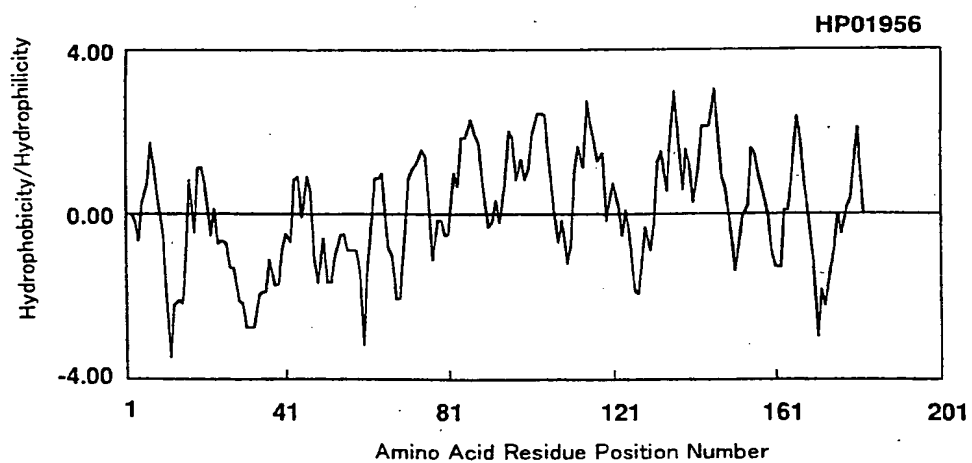
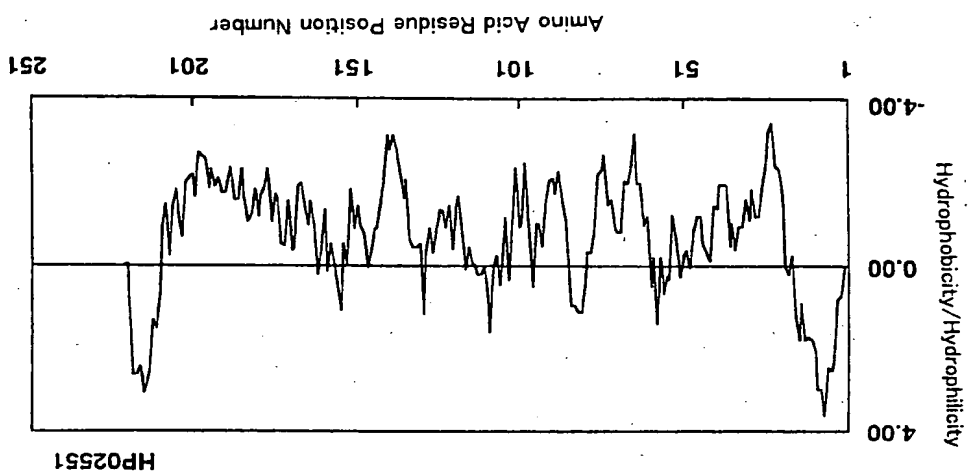


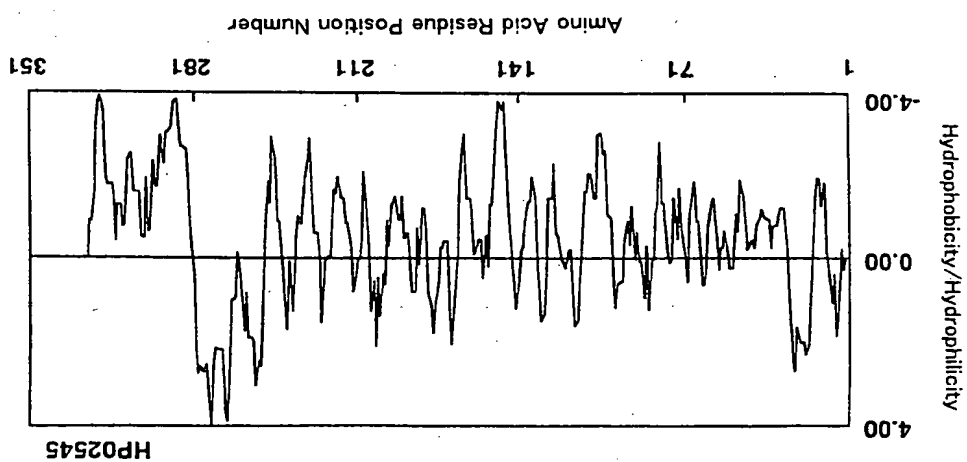
Fig.22

Fig. 24



24/50

Fig. 23



23/50



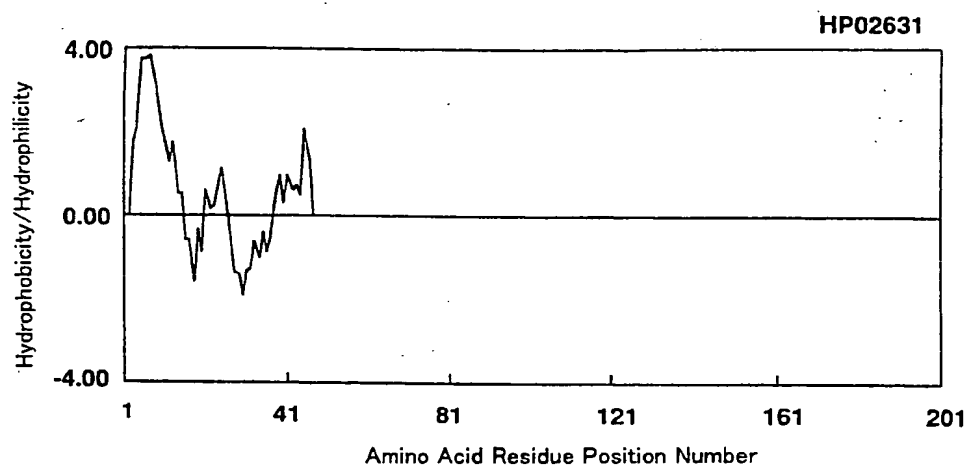


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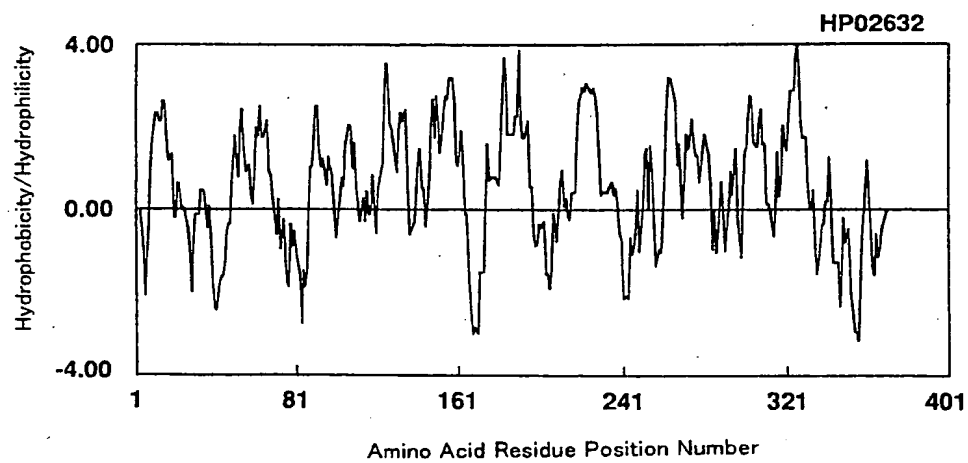


Fig. 26

Fig. 28

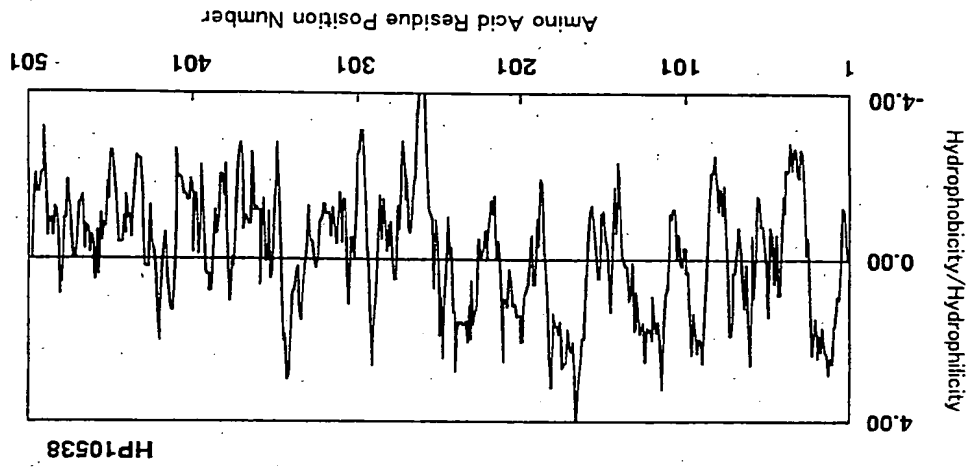
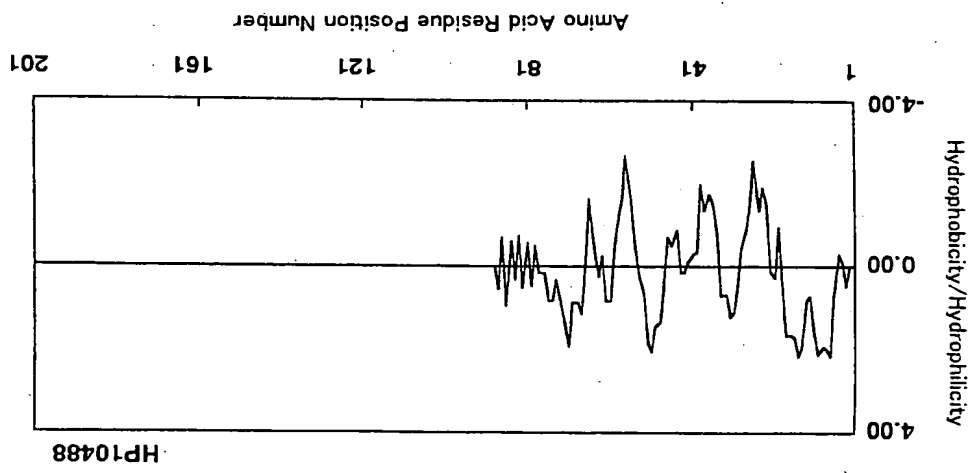


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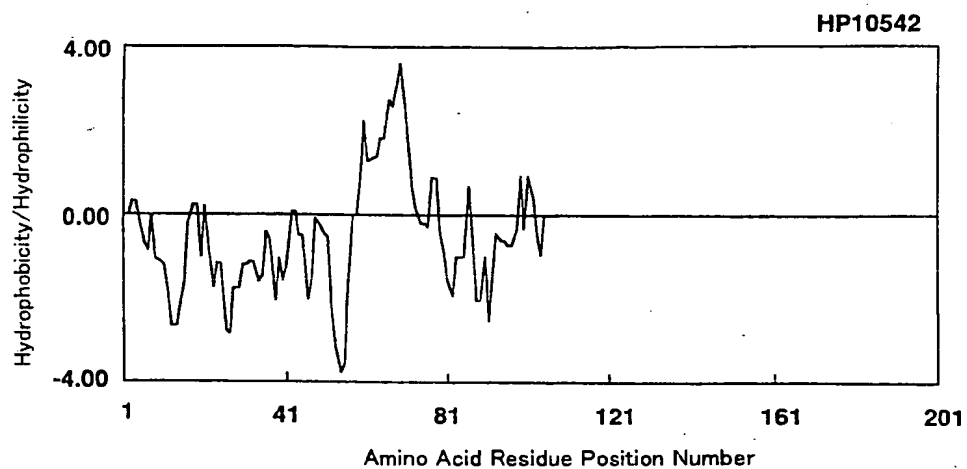


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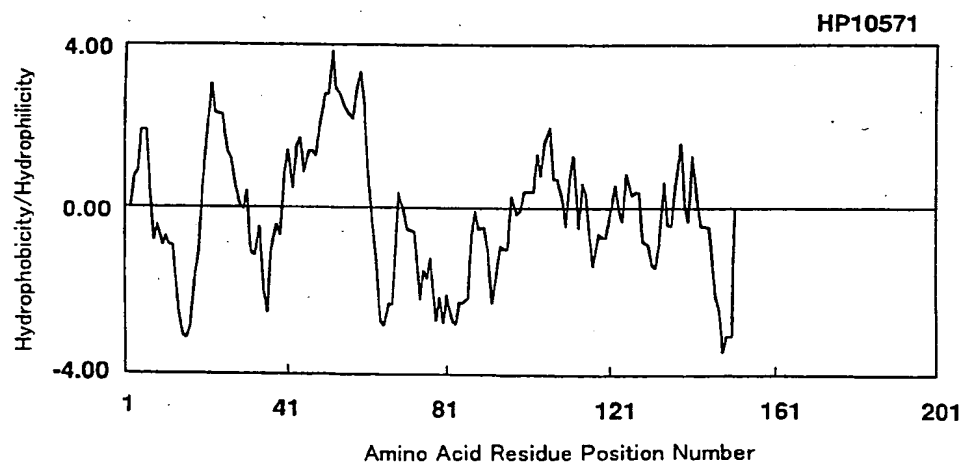


Fig. 30

32/50

31/50

Fig. 32

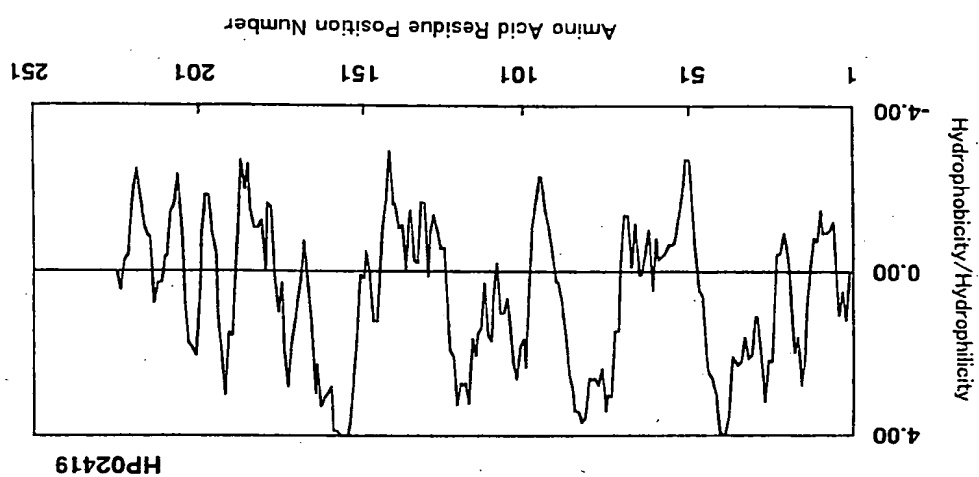
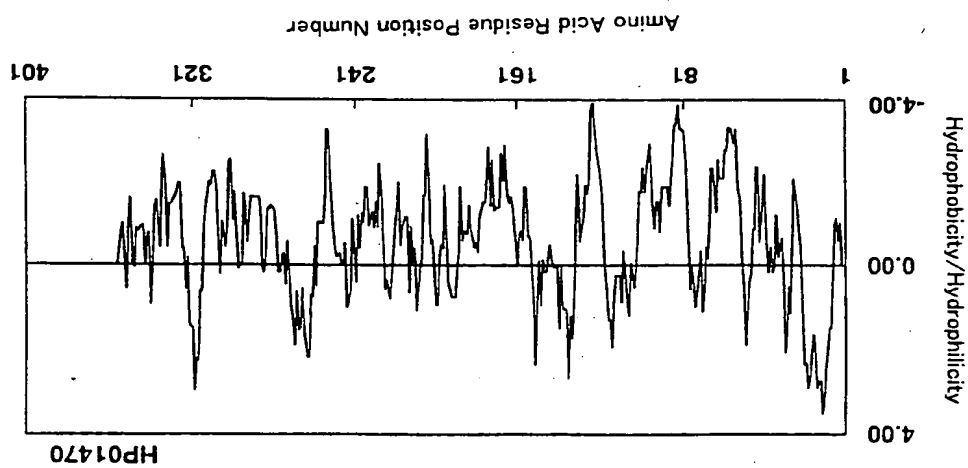


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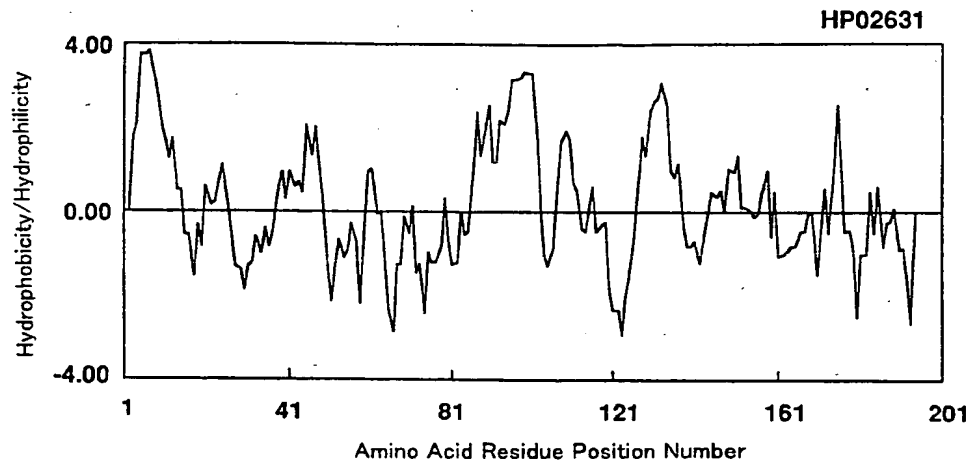


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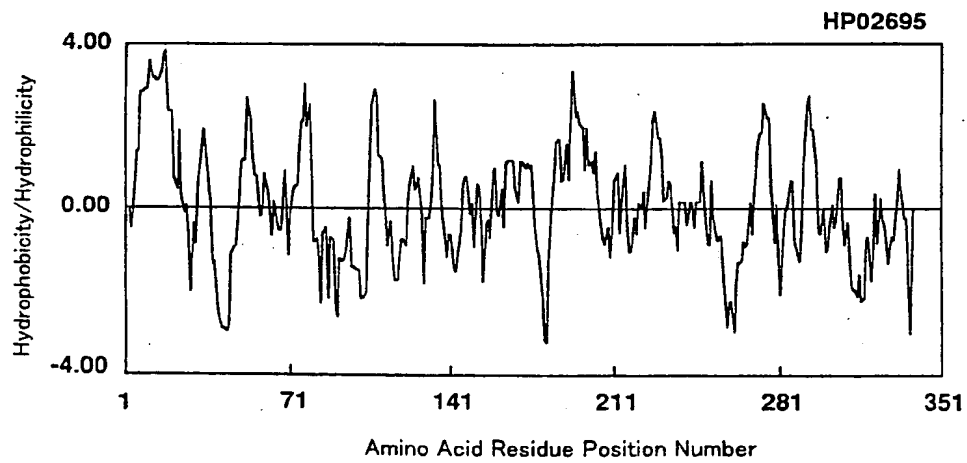
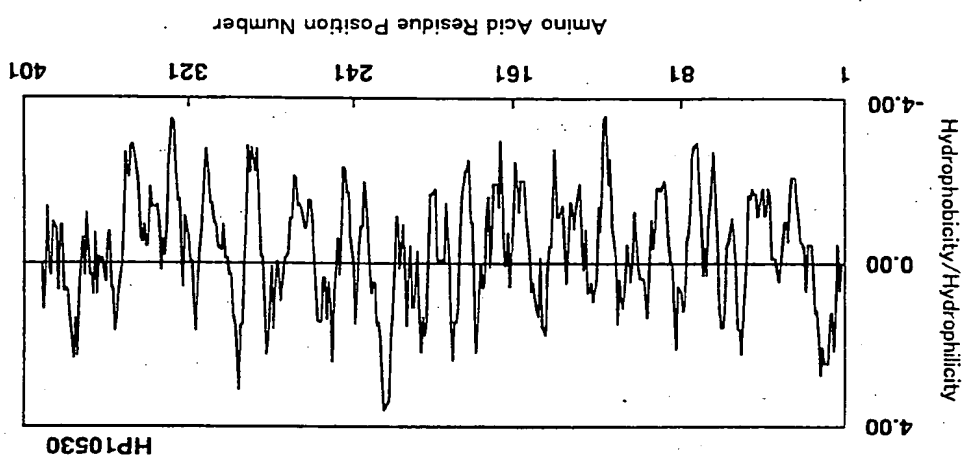


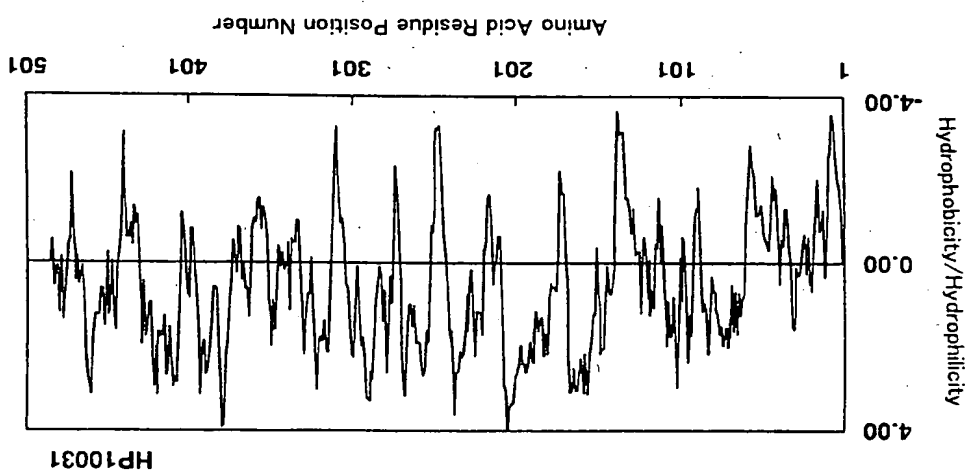
Fig. 34

Fig. 36



36/50

Fig. 35



35/50

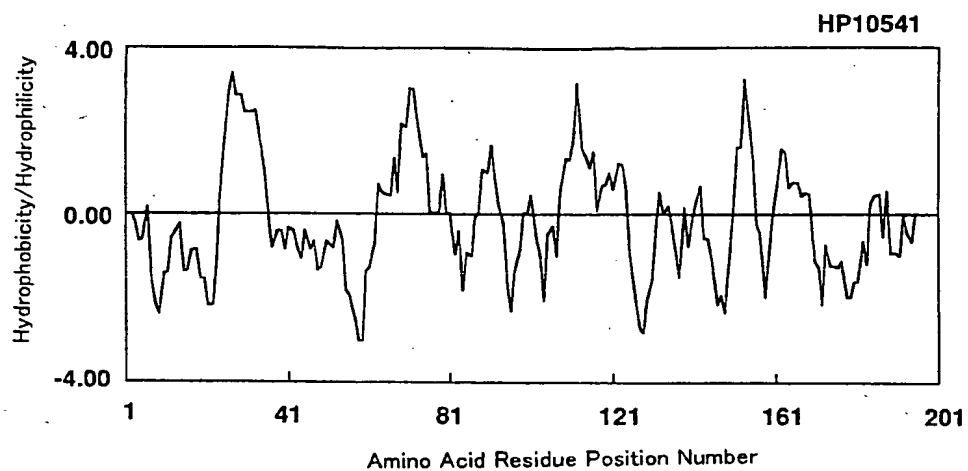


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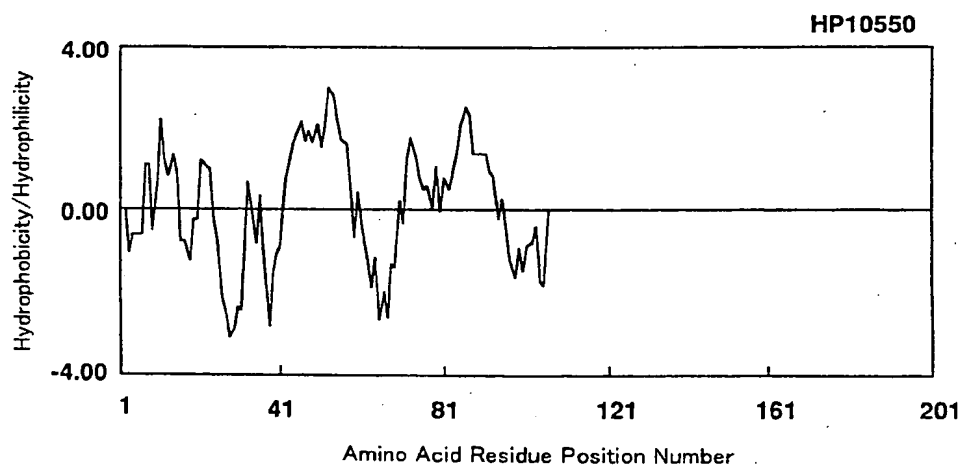


Fig. 38

Fig. 40

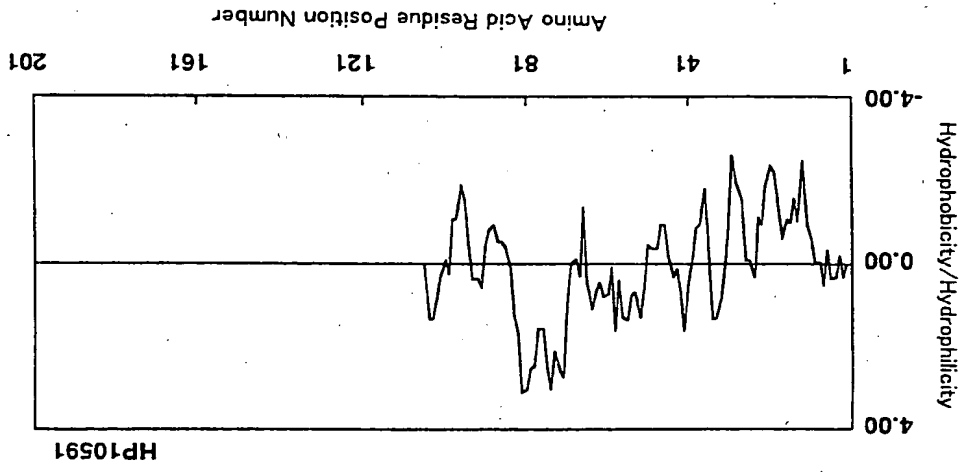
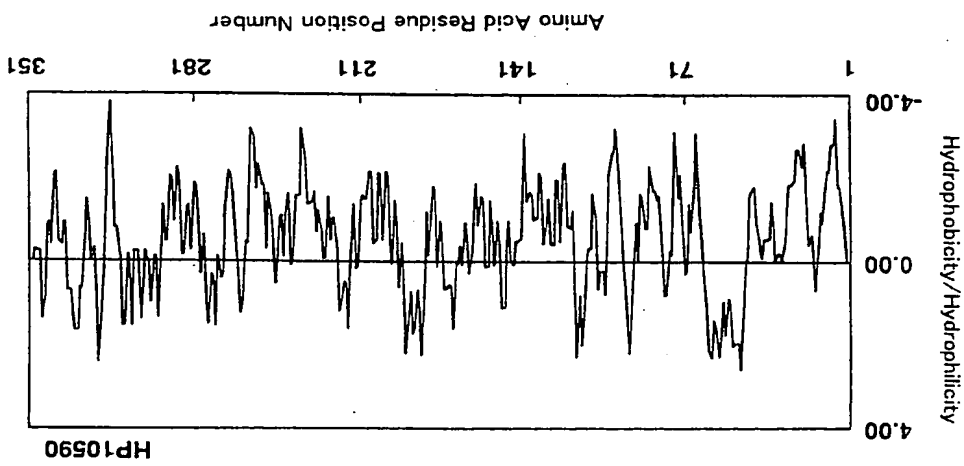


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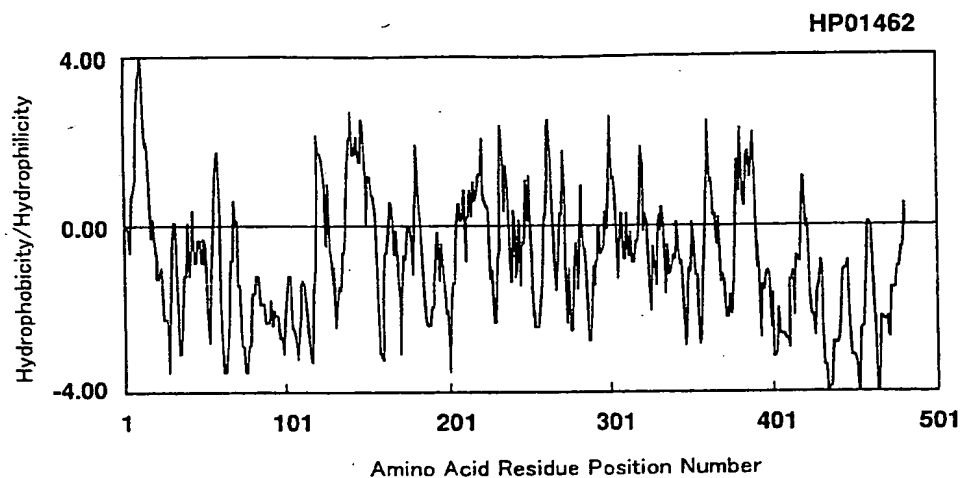


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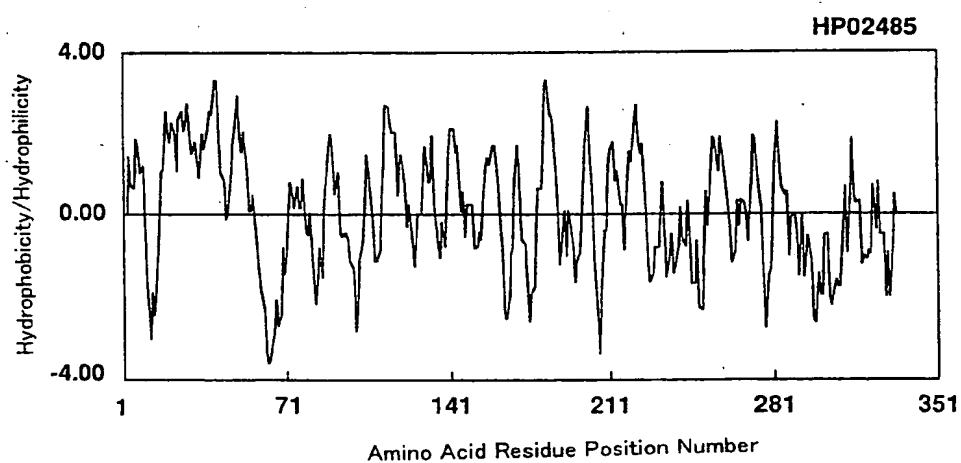


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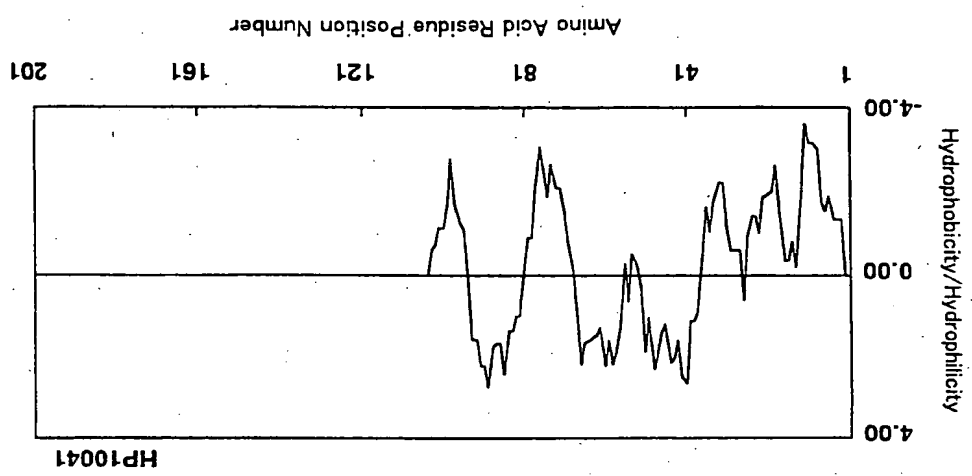


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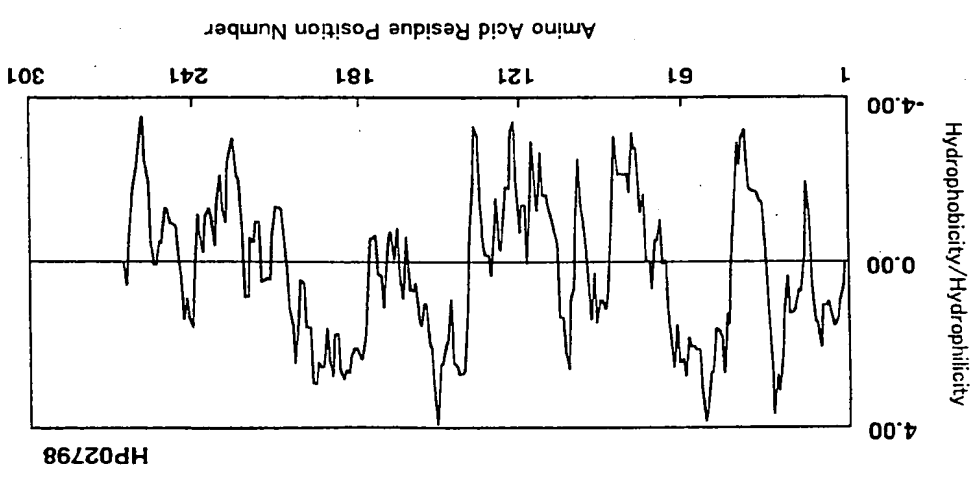


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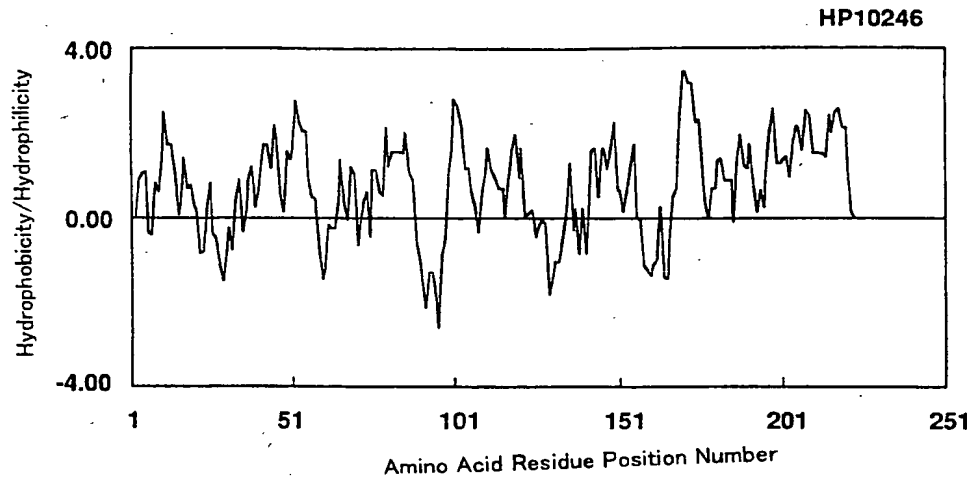


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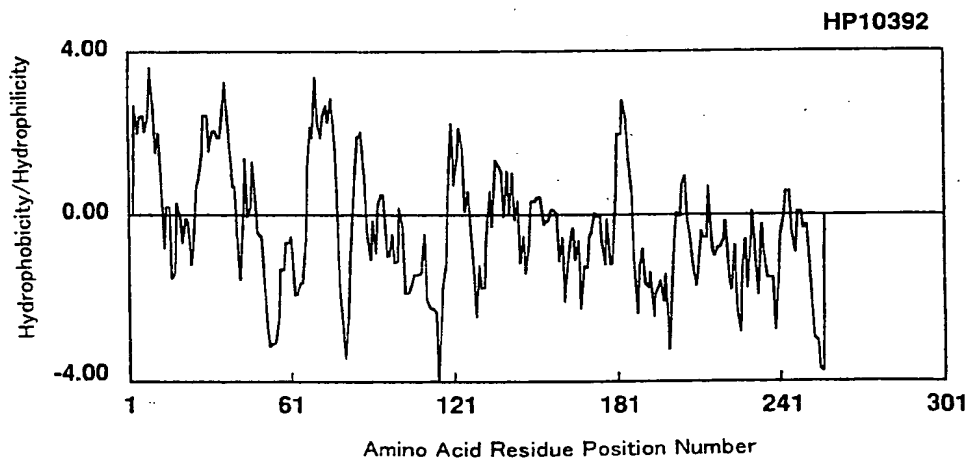


Fig. 46

Fig. 48

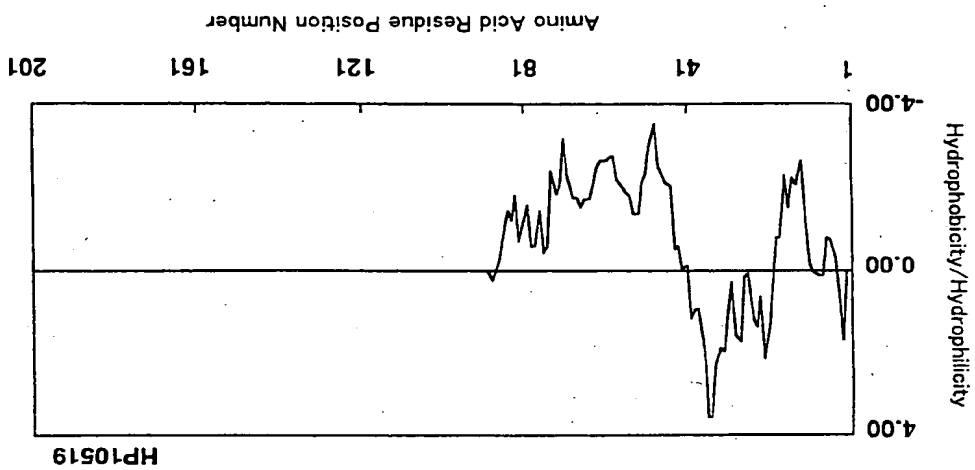
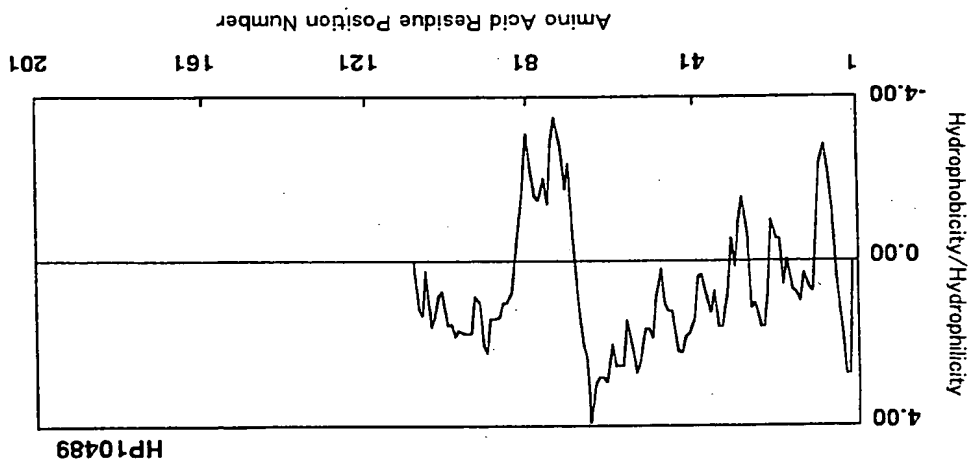


Fig. 47



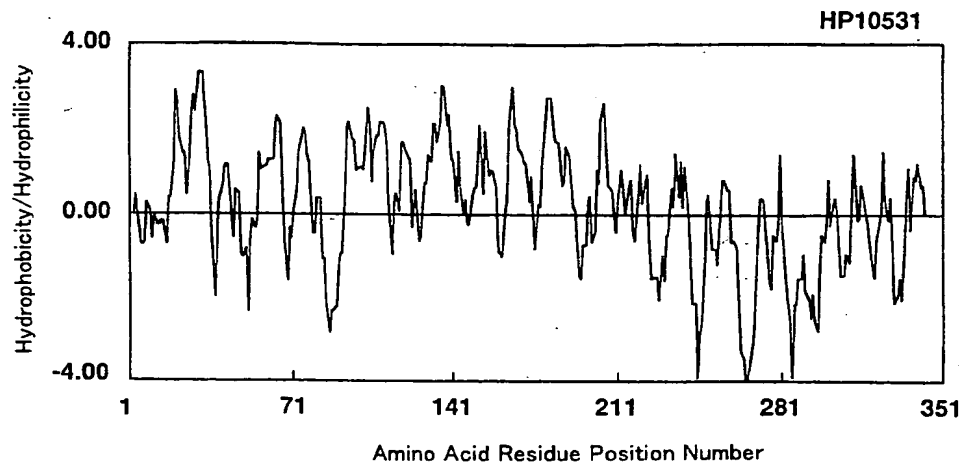


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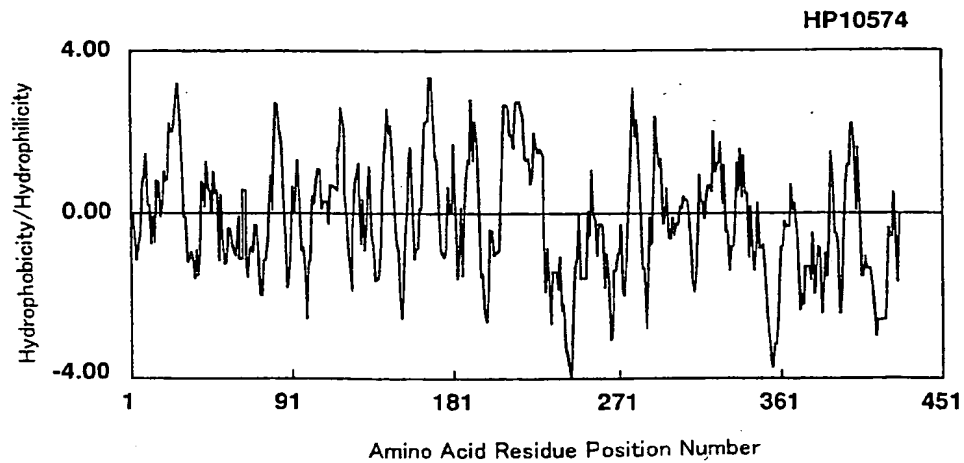


Fig. 50

1/177

2/177

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3/177

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4/177

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5/177

WO 00/05367

PCT/JP99/03929

6/177

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7/177

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8/177

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9/177

10/177

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11/177

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	aatgaanaa gtaaacaaa gtttatgta cagaaattt ttgtccacc aaaccttca	300

12/177

5	gatatgaag ctgtgtgaa agaggaanaa cctgatgaat taatgattc caaatgaga	360
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	gttccactga atgacatca gaaagatgga cctatggcca aaccacacag tgttcaact	480
	aatgatccg aaaaagaa actaatgaa gattgtaaa gactcaagg agaatgatg	540
	aagttacag aagaanaatg gacatgaga gatgaagtgt taagttcag aagagttaga	600
10	caatggata aacotggatc aactccaact gactcttca gagaataatg caacagcct	660
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	atcttg	726
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	<211> 792	
	<212> DNA	
	<213> Homo sapiens	
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	atgtctaga ttggttact ctatccagat tgccttgcg caatgtttgg aaaaatcaa	180
	tatggacca cagaagaa ttcaacagaa cttaagata atgtgaaat gttatcttg	240
	ccttcaagaa agcttggcg tctacagta agtccactt ttattaaata taaatcaag	300
25	ccattctgta aaaaactgt ttcctggtg aaagcagtg gctgtgccag agtaattgt	360
	cttccagaa gtatcatca taaggaat gactcgagc ttccgtgtae tccctcccg	420
	tactactta cacttccat gaaaaaagt gttaaaata aaataaagag ccttaactg	480
	gaagaaatg aaaaagccg gtgcattcct gaatatagtg attccaggtt ttgtaacgc	540
	attccggag gaggtatcac aaaaacatc tatgatgaa gctgtcttaa agaatccaa	600
30	atggcagtc tgcrgaaat tgtttcaga ggggacaaa tccagatgc attagctct	660
	gtttagata ttaatgagt gtttcagata ctcaaacac taagtgatga cccacagta	720
	tctgcctcac gttggaatat aacaaattct tggagattac tcttggcag tgccttcc	780
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	<211> 336	
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13/177

14/177

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 ggcgcaccg ccaaacctgc gccccaagct acaccggag cgcgacctc cccagagaa 120  
 caccgcctgt tgaagacctg ctggagctgt cgcgtcttt ctgggttgg gctgagtggg 180  
 gggggcgggt aaggttactg ggtggcaagg aagcccatga agatgggata ccccagct 240  
 ccatggacca ttacagat ggtcaccg ctcagcctg ccactggg tatcgttc 300  
 atggcagacc ccaagggaa ggcctaccg gttgtt 336  
  
 <210> 16  
 <211> 438  
 <212> DNA  
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10

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 gcaagacct caatttgc atgtgtctg gtggaagagt ttgtgtagc agaagctgc 180  
 tctcatgt ctatttcc ggtanaact accctgagt gtgtccac aggatatga 240  
 gagaatca catgcagtc atcaagaa atgagttca aagctgcc ctacgtttg 300  
 atggacaac gctattttg gaagtccaa ggggctgtc ttgtgtggc cctgacttc 360  
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20

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25

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 tttctctga taattccga atgtcttcag agagcctgc atggattgt tcatctt 180  
 ttccataga gaaccacac cttaattgc ctgcacctg tcttcaagg gatgtttat 240  
 actgagata cctgggaagt atttgtac tgcaggagc tggagtgtc ctgcattac 300  
 cttctctgc cctactct gctagtgta aactgttt ttttacct gactgtgga 360

35

accaatctg gcattaac aaagcaaat gaattattat ttctcatgt ttatgaattt 420  
 gatgaatga tgtttccaa gaactgagg tctctactt gtgatttaag gaacacagct 480  
 cgaaccagc actgacgtgt gtgtaactgg tgtgtgacc gtttcgacca tcactgtgtt 540  
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 ttgacggct cggctggcac cgtcgcaat gtgagacca cttttctggt ccaattgttg 660  
 gtgatgtcag attatacca ggaacttao atcgatgac ttggacacct caatgttatg 720  
 gacaggct ttattacca gtaactgttc ctgactttc cagcgattgt ctctatctg 780  
 ggccttctg tggctctag ctactctg ggtgtgacc ttgtgtttgt cctgtatctg 840  
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 tgtcccttg tggctggcc tccgtcaga ggcaccaag tccaccgaa catcactc 960  
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 aagaacaaag aa 1032

10

<210> 18  
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15

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 ctgagccag aggcaggag gtccctggag aaggagaaa acagctaat gacaaagcc 180  
 tccactacg aagagaaat gaagtctt cggcagaga accggaaga catgtctc 240  
 tctgtgcca ttttacct cctgacgct gtatagcct actggccat g 291

25

<210> 19  
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 <213> Homo sapiens

30

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 aagctcgat tgaacctta tcaattgata tggcagaga tgaactctga aaatgagga 180  
 ctacagagg aattaaata aactgttt gacactga ttgaattct gcaaaatca 240

35

15/177

catctcgtat tccagagaga ttcagagagc ttgggacctg aaataaact cagagaaat 300  
ccaactcgtg ctcttgctt ttgtatatat gcatatgttt gtcatgcat gcaactctgt 360  
gtatctcgtt tt 372

5 &lt;210&gt; 20

&lt;211&gt; 981

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

10 &lt;400&gt; 20

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gggtcggccg tggaggtgaa ggtaccacaa ggcgcgttga gcaagccct gggagagaa 120  
gcgcagctga cctgaaccta cagcagctcg gtggagagaa gcttcgcct ggaatggagc 180  
tttgccagc ctggagaaac catctctgag tccatccaa tctgtact caacatggc 240  
catctgac caactgttc taagtcaaa cgggtcagcc tgccttga cccccaca 300  
gtgggggtg ccaaatgaa actgactgac gtccacct catatctg aacttactc 360  
tgcagatga acaaccacc agattctac acaatgggt tgggtctat caacttact 420  
gtgcgttc cccccagtaa tccctatgc agtcagatg gacaacctc tgtggagagc 480  
tctaccgac tgaatgagc ctctccgag ggggtccta agcaggtga caactgggtg 540  
cgtctgaa ctcttcctac acctctcct ggcagatag ttcagatga ggtgtctg 600  
cagtcattc tcaacaacct ctccctgac tccctggga cctacgctg tgtggcacc 660  
aaccaatg gcaatgac ctgtgagctg acctctcg tgaccgaac ctcccaagc 720  
cgaatggccg gaagctctgt tgggtgtc ctgggcgtg tgtgtctc agttgcgtg 780  
ttctgcctg tcaagttcaa gaaagagagg gggagagagc caagggagac atatgggt 840  
agtgaactc gggagatgc catgctcct gggatctcg agcaactg tatgaggt 900  
gattcagca aggggtcct ggaagacc tgcctcgaa gcaaccgtgac gacacaaag 960  
tcaagctcc ctatgtcgt g 981

&lt;210&gt; 21

30 &lt;211&gt; 510

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

35 &lt;222&gt; (66)...(443)

16/177

&lt;400&gt; 21

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ctgc atg gcc aag tac ctg gcc cag atc att gtg atg ggc gtc cag gtg 110  
Met Ala Lys Tyr Leu Ala Gln Ile Ile Val Met Gly Val Gln Val 15

1 5 10 15

gtg ggc aag gcc ttc gca cgg gcc ttg cgg cag gag ttt gca gcc agc 158  
Val Gly Arg Ala Phe Ala Arg Ala Leu Arg Gln Gln Phe Ala Ala Ser 30

20 25 30

10 cgg gcc gca gct gat gcc cga gga cgc gct gga cac cgg tct gca gcc 206

Arg Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala 40

35 40 45

gct tcc aac ctg tcc ggc ctg agc ctg cag gag gca cag aat ctg 254  
Ala Ser Asn Leu Ser Gly Leu Ser Leu Gln Gln Ala Gln Ile Leu 60

15 aac gtg tcc aag ctg agc cct gag gag gtc cag aag aac tat gaa cac 302

Asn Val Ser Lys Leu Ser Pro Gln Gln Val Lys Asn Tyr Gln His 70

65 70 75

20 tta ttt aag gtg aat gat aaa tcc gtg ggt ggc tcc ttc tac ctg cag 350

Leu Phe Lys Val Asn Asp Lys Ser Val Gly Ser Phe Tyr Leu Gln 80

85 90 95

tca aag gtg gtc cgc gca aag gag cgc ctg gat gag gaa ctg aaa atc 398  
Ser Lys Val Val Arg Ala Lys Gln Arg Leu Asp Gln Leu Lys Ile 100

105 110

25 cag gcc cag gag gac aga gaa aaa ggg cag atg ccc cat acg tgactgtc 450

Gln Ala Gln Gln Asp Arg Gln Lys Gly Gln Met Pro His Thr 115

120 125

gtcccccgc ccacccgcgc cgcctctaat ttatagcttg gtaataaatt tctttctgc 510

30 &lt;210&gt; 22

&lt;211&gt; 697

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

35 &lt;221&gt; CDS

17/177

18/177

&lt;222&gt; (104)...(499)

&lt;400&gt; 22

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cgcgcgcc tgggtctg ggcctagcg cgcctcacc gcc atg gca ggc atc 115

Met Ala Gly Ile

1

aaa gct ttg att agt ttg tcc ttt gga gga gca atc gga ctg atg ttt 163

Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile Gly Leu Met Phe

5 10 15 20

ttg atg ctt gga tgt gcc ctt cca ata tac aac aaa tac tgg ccc etc 211

Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys Tyr Trp Pro Leu

25 30 35

ttt gtt cta ttt ttt tac atc ctt tca cct att cca tac tgc ata gca 259

Phe Val Leu Phe Tyr Ile Leu Ser Pro Ile Pro Tyr Cys Ile Ala

40 45 50

aga aga tta gty gat gat aca gat gct atg agt aac gct tgt aag gaa 307

Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn Ala Cys Lys Glu

55 60 65

ctt gcc atc ttt ctt aca acg ggc att gtc gty tca gct ttt gga etc 355

Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser Ala Phe Gly Leu

70 75 80

cct att gta ttt gcc aga gca cat ctg att gag tgg gga gct tgt gca 403

Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp Gly Ala Cys Ala

85 90 95 100

ctt gtt ctc aca gga aac aca gtc atc ttt gca act ata cta ggc ttt 451

Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr Ile Leu Gly Phe

105 110 115

ttc ttg gtc ttt gga agc aat gac gcc ttc agc tgg cag cag tgg tga 500

Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp Glu Trp

120 125 130

aagaattac tgaatttg tcaattggac ttcctgtcat ttgttgcca ttaacgaca 560

caggagatgg ggcattat gctgaatggt atagcagcc ttctgggggt atttaggtg 620

ctcccttc actttttg taagctact attttcacg agacttgcg aagattaaa 680

aggattttct cttttg 697

&lt;210&gt; 23

&lt;211&gt; 1619

&lt;212&gt; DNA

5 &lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (287)...(1015)

10 &lt;400&gt; 23

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tgggttag taactgggt ggcagaggt tctgaccca ggggtggc caccagaccg 120

gtgacacgc ggcagaggtt agggctggg agcggagc ctggcctgt cctagagctc 180

ggcagagcg tgcgcctgt cgtcccccgc cccagtagc caaacgcgc cggggggc 240

gccccctc tgcgtgtct ctcagtagc gtcagtagc ggggc atg ggc aag 295

Met Ala Lys

1

cac gag cag atc ctg gtc etc gat ccg ccc aca gac etc aaa ttc aaa 343

His Glu Gln Ile Leu Val Leu Asp Pro Thr Asp Leu Lys Phe Lys

20 5 10 15

ggc ccc ttc aca gat gta gtc act aca aat ctt aaa ttg cga aat cca 391

Gly Pro Phe Thr Asp Val Val Thr Thr Asn Leu Lys Leu Arg Asn Pro

20 25 30 35

tcg gat aga aaa gty tgt ttc aaa gty aag act aca gca cct cgc cgg 439

Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala Pro Arg Arg

40 45 50

tac tgt gty agg ccc aac agt gga att att gac cca ggg tca act gty 487

Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly Ser Thr Val

55 60 65

act gtt tca gta atg cta cag ccc ttt gat tat gat ccg aat gaa aag 535

Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro Asn Glu Lys

70 75 80

agt aac cac aag ttt atg gta cag aca att ttt gct cca cca aac act 583

Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro Pro Asn Thr

85 90 95

19/177

100 tca gat atg gaa gct tgg aaa gag gaa aac cct gat gaa tta atg 631  
Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp Glu Leu Met  
105 110 115  
gat tcc aaa tgg aga tgc gta ttt gaa atg ccc aat gaa aat gat aaa 679  
Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu Asn Asp Lys  
120 125 130  
ttg aat gat atg gaa cct agc aaa gct gtc cca ctg aat gaa tct aag 727  
Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn Ala Ser Lys  
135 140 145  
caa gat gga cct atg cca aaa cca agc agt gtt tca ctt aat gat acc 775  
Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu Asn Asp Thr  
150 155 160  
gaa aca agg aaa cta atg gaa gag tgt aaa aga ctt cag gga gaa atg 823  
Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Glu Gly Glu Met  
165 170 175  
atg aag cta tca gaa gaa aat cgg cnc ctg aga gat gaa ggt tta agg 871  
Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu Gly Leu Arg  
180 185 190 195  
ctc aga aag gta gca cat tgg gat aaa cct gga tca acc tca act gaa 919  
Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala  
200 205 210  
tcc ttc aga gat aat gtc acc agt cct ctt cct tca ctt ctt gtc gta 967  
Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu Leu Val Val  
215 220 225  
att gaa gcc att ttc att gga ttc ttt cta ggg aaa ttc atg ttg 1012  
Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Glu Lys Phe Ile Leu  
230 235 240  
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acagtgcat ataggtttg octtaatga tctctacag ttaaaaaa caataaac 1190  
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gcacatgag tcttaatga aatcaataa taagaatg tttctctt gtgttttaa 1310  
taagaatga agaatgttc agagtctgt aatgttat ttaataacc cttaaat 1370  
tatctgtgc tgtacctct tgaatatga ttatctaga ttgctaacc caatctaa 1430  
ggaatgcaa agagttatc ctgtggaaa tggtagcctc taagaatgaa atttcttc 1490

20/177

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ttaacagat 1619  
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gacc atg ttc gtc ccc tgc ggg gag tgg gcc ccc gac ctt gcc ggc ttc 109  
Met Phe Val Pro Cys Gly Glu Ser Ala Pro Asp Leu Ala Gly Phe  
1 5 10 15  
acc ctc cta atg cca gaa gta tct gtc gga aat gtc ggc cag ctt gca 157  
Thr Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Glu Leu Ala  
20 25 30  
atg gat ctg att att tct aca ctg aat atg tct aag att ggt tac ttc 205  
Met Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe  
35 40 45  
tat acc gat tgt ctt gtc cca atg gtc gga aac aat cca tat gcg acc 253  
Tyr Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr  
50 55 60  
aca gaa gga aat tca aca gaa ctt agc ata aat gct gaa gtc tat tca 301  
Thr Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser  
65 70 75  
ttg cct tca aga aag ctg gtc gct cta cag tta aga tcc att ttt att 349  
Leu Pro Ser Arg Lys Leu Val Ala Leu Glu Leu Arg Ser Ile Phe Ile  
80 85 90 95  
aag tat aaa tca aag cca ttc tgt gaa aaa ctg ctt tcc tgg gtc aaa 397  
Lys Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys  
100 105 110

21/177

5 agc agt ggc tgt gcc aga gtc att gtt ctt tcg agc agt cat tca tat 445  
 Ser Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr  
 115 120 125  
 cag cgt aat gat cgt cag ctt cgt agt act ccc ttc cgg tac cta ctt 493  
 Gln Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu  
 130 135 140  
 aca cct tcc atg caa aaa agt gtt caa aat aaa ata aag agc att aac 541  
 Thr Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn  
 145 150 155  
 10 tgg gaa gaa atg gaa aaa agc cgg tgc att cct gaa ata gat gat tcc 589  
 Trp Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser  
 160 165 170 175  
 gag ttt tgt atc cgc att ccg gga gga ggt atc aca aaa aca ctc tat 637  
 Glu Phe Cys Ile Arg Ile Pro Gly Gly Ile Thr Lys Thr Leu Tyr  
 180 185 190  
 gat gaa agc tgt tct aaa gaa atc caa atg gca gtt cty cty aaa ttt 685  
 Asp Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe  
 195 200 205  
 gtt tca gaa ggg gac aac atc cca gat gca tta ggt ctt gtt gag tat 733  
 Val Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr  
 210 215 220  
 ctt aat gag tgg ctt cag ata ctc aaa cca cca att agc gat gac ccc aca 781  
 Leu Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr  
 225 230 235  
 25 gta tct gcc tca cgg tgg aaa ata cca agt tct tgg aga tta ctc ttt 829  
 Val Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe  
 240 245 250 255  
 ggc agt ggt ctt ccc cct gca ctt ttc tgatctaatt tctgtttat acct 880  
 Gly Ser Gly Leu Pro Pro Ala Leu Phe  
 260  
 30 tatecccaaa acactacta ccaacacgc tgtaaact tctatacaaa aaatgtgat 940  
 gatctgtat taggaatta ctttcacgt aaatataca gaaaaagt taaggctc 1000  
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 ctaagt 1066

22/177

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 1 ggg tct cgg ttg tcc cag cct ttt gag tcc tat atc act gcg cct ccc 104  
 Gly Ser Arg Leu Ser Gln Pro Phe Glu Ser Tyr Ile Thr Ala Pro Pro  
 5 10 15  
 15 ggt acc gcc gcc gcc ccc aaa cct gcg ccc cca gct aca ccc gga 152  
 Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Ala Thr Pro Gly  
 20 25 30  
 ggg ccg acc tcc cca gca gaa cac cgc ctg ttg aag acc tgc tgg agc 200  
 Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp Ser  
 35 40 45  
 tgt cgc gtg ctt tct ggg ttg ggg ctg atg ggg gcg ggc ggg tac gtg 248  
 Cys Arg Val Leu Ser Gly Leu Met Gly Ala Gly Tyr Val  
 50 55 60 65  
 25 tac tgg gtg gca cgg aag ccc atg aag atg gga tac ccc ccg agt cca 296  
 Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser Pro  
 70 75 80  
 tgg acc att acg cag atg gtc atc ggc ctc agc att gcc acc tgg ggt 344  
 Trp Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp Gly  
 85 90 95  
 30 atc gtt gtc atg gca gac ccc aaa ggg aag gcc tac cgc gtt gtt t 390  
 Ile Val Val Met Ala Asp Pro Lys Gly Lys Ala Tyr Arg Val Val  
 100 105 110  
 gaagtaaca ccaagtgaac tgtattctgt cttgtccct ttcccctga ccaacacgc 450  
 aggcacggaa ttaattgggt gttctggaca gaaattgta catggacaga catcactact 510



23/177

gtgagatctaa caagactgag aagaaatcgt tatgttgcga ttctcttgct atggagtgt 570  
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ggtgagcggt agctagagcc gcagagccccc gccggccctt cctccagagc cctggagac 180  
ccgcagaagt agctcagctc cctagccgcg aaaaacatct cgaattttct cgtcttggca 240  
aaggggagct cctatagat cctcctgctc aataggaac tccggcctc cctggcctga 300  
cctggaaact ctgggaaggc tgcagaatga gtgcgcctc tgcgtccga cggagagcag 360  
aggtcttgg agtagtccc tctgttcga caggtgcgac acttggcgt cc atg ctt 418  
Met Leu  
  
gcc ggt gcc ggg agt cct ggc ctg ccc cag ggc cgc cag ctg tgc tgg 1  
Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu Cys Trp  
5 10 15  
ctg ctg tgt gct ttc acc tta aag ctg tgc caa gca gag gct ccc gtcg 514  
Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Gln Ala Pro Val  
20 25 30  
cag gaa gag aag ctg tca gca agc acc tca aat ttg cca tgc tgg ctg 562  
Gln Gln Gln Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys Trp Leu  
35 40 45 50  
gtg gaa gag tct gty gta gca gaa gag tgc tct cca tgc tct aat ttc 610  
Val Gln Gln Phe Val Ala Gln Gln Cys Ser Pro Cys Ser Asn Phe  
55 60 65  
cgg gct aaa act acc cct gag tgt ggt ccc aca gga tat gta gag aaa 658  
Arg Ala Lys Thr Thr Pro Gln Cys Gly Pro Thr Gly Tyr Val Gln Lys

24/177

atc aca tgc agc tca tct aag aga aat gag ttc aaa agc tgc cgc tca 70  
Ile Thr Cys Ser Ser Lys Arg Asn Gln Phe Lys Ser Cys Arg Ser 80  
85 90 95  
gct ttg atg gaa caa cgc tta ttt tgg aag ttc gaa ggg gct gtc gtc 754  
Ala Leu Met Gln Gln Arg Leu Phe Thr Lys Phe Gln Gly Ala Val Val  
100 105 110  
tgt gtc gcc ctg atc ttc gct tgt ctt gtc atc att cgt cag cga caa 802  
Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln Arg Gln  
115 120 125 130  
ctg gac aga aag gct ctg gaa aag gtc cgg aag caa atc gag tcc ata 850  
Leu Asp Arg Lys Ala Leu Gln Lys Val Arg Lys Gln Ile Gln Ser Ile  
135 140 145  
tagctacatt ccacccctgt atccctggtc tttagaacct tatctcagac agtgaagt 910  
aaatgagctg attgcacac ttggtctttt ggaacctgtt ggtgaaatcc cctttccc 970  
attcttctt ttcaagatcat taatgagcag aataaaaga gtaaatgtt t 1021  
  
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gcccgagccg gggggagccc cgtgtccccc tccggccctg ctgaaactca cgtccacctt 120  
ccagggtccc agcccacag gaaatcccg accagagccg cccaggagcc agatccaggc 180  
tccctgaga accatgtccg gcagctactg gtcaatgccag gcaacactg ctggccaaga 240  
ggagctgtgt ttgaaatcat ctgtgaatgt tgggaagagg aatgcacag ctgcggctg 300  
aaatatacc aaccaagaga aatctcag atg gac ttt ctg gtc ctg ttc ttg 354  
Met Asp Phe Leu Val Leu Phe Leu  
1 5  
ttc tac ctg gct tcc gtc ctg atg ggt ctt gtt ctt atc tgc gtc tgc 402

25/177

Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys  
 10 15 20  
 tgg aaa acc cat agc ttg aaa ggc ctg gcc agg gga gca cag ata 450  
 Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile  
 25 30 35 40  
 ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga tgg 498  
 Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu  
 45 50 55  
 ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac 546  
 Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His  
 60 65 70  
 ctg gtc ttg caa ggg atg gtt tat act gag tac acc tgg gaa gta ttt 594  
 Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe  
 75 80 85  
 ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc 642  
 Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro  
 90 95 100  
 tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga 690  
 Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Thr Leu Thr Cys Gly  
 105 110 115 120  
 acc aat cct gcc att ata aca aca gca aat gaa tta tta ttt ctt cat 738  
 Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His  
 125 130 135  
 gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tat 786  
 Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser  
 140 145 150  
 act tgt gat tta agg aaa cca gct cga tcc aag cac tgc agt gtg tgt 834  
 Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys  
 155 160 165  
 aac tgg tgt gtg cac cgt ttc gac cat cac tgt gtt tgg gtg aac aac 882  
 Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn  
 170 175 180  
 tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc 930  
 Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr  
 185 190 195 200

26/177

ttg acg gcc tgg gct gcc acc gtc gcc att gtg agc acc act ttt ctg 978  
 Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser Thr Thr Phe Leu  
 205 210 215  
 gtc cac ttg gtg atg tta tta tta tta tta tta tta tta tta tta tta 1026  
 Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu Thr Tyr Ile Asp  
 220 225 230  
 gac ctt gga cgc ctc cat gtt atg gac acg gtc ttt ctt att cag tac 1074  
 Asp Leu Gly His Leu His Val Met Asp Thr Val Phe Leu Ile Gln Tyr  
 235 240 245  
 ctg ttc ctg act ttt cca cgg att gtc ttc atg ctg ggc ttt gtc gtc 1122  
 Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu Gly Phe Val Val  
 250 255 260  
 GTT CTG AGC TTC CTC CTG GGT GGC TAC CTG TTT TTT GTC CTG TAT CTG 1170  
 Val Leu Ser Phe Leu Leu Gly Tyr Leu Leu Phe Val Leu Tyr Leu  
 265 270 275 280  
 gcg gcc acc aac cag act act aac gag tgg tac aga ggt gac tgg gcc 1218  
 Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg Gly Asp Trp Ala  
 285 290 295  
 tgg tgc cag cgt tgt ccc ctt gtg gcc tgg cct ccc gca gag ccc 1266  
 Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro Ser Ala Glu Pro  
 300 305 310  
 caa gtc ccc cgg aac att cac tcc cat ggg ctt cgg agc aac ctt caa 1314  
 Gln Val His Arg Asn Ile His Ser His Gly Leu Arg Ser Asn Leu Gln  
 315 320 325  
 gag atc ttt cta cct gcc ttt cca tgt cat gag agg aag aca gaa 1362  
 Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg Lys Gln Glu  
 330 335 340  
 tgaacagtgt atgactgct ttgagatgta gttcccggtt attaccatc gtggatcc 1420  
 tegttttcaa ag 1432  
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 <211> 601  
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27/177

<221> CDS  
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c atg act aaa aag aag cgg gag aat ctg gtc gtc cta gag atc gat 109  
Met Thr Lys Lys Arg Gln Asn Lys Val Ala Lys Ile Asp  
1 5 10 15  
ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag ggc gtc 157  
Gly Leu Gln Gln Lys Leu Ser Gln Cys Arg Arg Asp Leu Gln Ala Val  
20 25 30  
aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc aag agc tcc 205  
Asn Ser Arg Leu His Ser Arg Gln Leu Ser Pro Gln Ala Arg Arg Ser  
35 40 45  
ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag 253  
Leu Gln Lys Gln Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Gln  
50 55 60  
aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc 301  
Lys Gln Leu Lys Phe Leu Arg Gln Gln Asn Arg Lys Asn Met Leu Leu  
65 70 75 80  
tct gtc gcc atc ttt atc ctc ctg aag ctc gtc tat gcc tac tgg acc 349  
Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr  
85 90 95  
atg tggacttggc acttcccac aaccagaca ggttccact tggccct 400  
Met  
25  
tgatcagat caagcagga cttaagcct caatagacc aagtgcttg gttgttccc 460  
tcccaacctt gtttcaagg atgttctct ggcggccag gcttggcctt cctggactgc 520  
tgggggttc cgggttcca gaagacatg gtgtgtgcc ctccctagg caaaggaga 580  
30 ggcataaag aacaaagct g 601

<210> 29  
<211> 585  
<212> DNA  
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28/177

<220>  
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<222> (78)...(452)

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gcagctcag taagacc atg gct aag tcc tgg atg tct aag ggt tgc ttt 110  
Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe  
1 5 10  
ggt ttt aag cca aac tcc aaa aag aga atc tct ctg cca ata gag 158  
Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Gln  
15 20 25  
gac tat ttt aac aaa ggg aaa aat gag cct gag gac agt aag ctt cga 206  
Asp Tyr Phe Asn Lys Gly Lys Asn Gln Pro Gln Asp Ser Lys Leu Arg  
30 35 40  
ttc gaa act tat cag ttg ata tgg cag cag atg aaa tct gaa aat gag 254  
Phe Gln Thr Tyr Gln Leu Ile Trp Gln Gln Met Lys Ser Gln Asn Gln  
45 50 55  
cga cta caa gag gaa tta aat aaa aac ttg ttt gac aat ctg att gaa 302  
Arg Leu Gln Gln Gln Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Gln  
60 65 70 75  
ttt ctg caa aaa tca cat tct gga ttc cag aag aat tca aga gac ttg 350  
Phe Leu Gln Lys Ser His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu  
80 85 90  
ggc ggt caa ata aaa ctc aga gaa att cca act gct gct ctt gtt ctt 398  
Gly Gly Gln Ile Lys Leu Arg Gln Ile Pro Thr Ala Ala Leu Val Leu  
95 100 105  
ggt ata tat gag tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt 446  
Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg  
110 115 120  
ttt taattttt ttatctgtt agaatatgtt aaggacttgt ttgatgagc c 500  
Phe  
25  
tatttgct ctcctatttg taacaataaa ccaactatag ttatatatc atatttcaa 560  
35 aaacaataa aaattcctta tcttt 585

[illegible]

31/177

ttc ctg gaa aga ccc tcc tct gcc agc acc gtc acc acc aag tcc 1019  
 phe leu glu arg pro ser ser ala ser thr thr thr lys ser 310 315 320  
 aag ctc cct atg gtc gtc tgactctcc cgatccctga gggcgggtgag ggg 1070  
 lys leu pro met val val 325  
 gaattcaat aattaagtc tctgggtacc 1100  
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 <213> Homo sapiens  
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 Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
 20 25 30  
 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
 35 40 45  
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
 50 55 60  
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Trp Thr  
 65 70 75 80  
 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
 85 90 95  
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Gln  
 100 105 110  
 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala  
 115 120 125  
 Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala  
 130 135 140  
 Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His  
 145 150 155 160  
 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Thr Gly Phe Leu

32/177

Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val  
 165 170 175  
 180 185 190  
 Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro  
 195 200 205  
 Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser  
 210 215 220  
 Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val  
 225 230 235 240  
 Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val  
 245 250 255  
 Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe  
 260 265 270  
 Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp  
 275 280 285  
 Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr  
 290 295 300  
 Glu Ala Ala Val Leu Leu Phe Tyr Arg  
 305 310  
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 <211> 229  
 <212> PRT  
 <213> Homo sapiens  
 <400> 32  
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala  
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 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu  
 20 25 30  
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Cys Phe  
 35 40 45  
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val  
 50 55 60  
 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

33/177

65 70 75 80  
Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr  
85 90 95  
Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe  
100 105 110  
Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn  
115 120 125  
Met Gly Glu Gln Ala Gln Glu Asp Tyr Lys Lys Tyr Ile Thr  
130 135 140  
Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile  
145 150 155 160  
Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu  
165 170 175  
Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe  
180 185 190  
Asp Arg Val Asn Phe Thr Ser Met Val Asn Leu Val Met Val Val  
195 200 205  
Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys  
210 215 220  
Arg Lys Ser Arg Thr  
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<210> 33  
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<212> PRT  
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Leu Leu Leu Leu Leu Pro Pro Pro Cys Pro Ala His Ser Ala Thr  
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Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala  
35 40 45  
Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

34/177

50 55 60  
Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Tyr Trp Gln Lys  
65 70 75 80  
Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro  
85 90 95  
Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe  
100 105 110  
Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr  
115 120 125  
Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser  
130 135 140  
Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp  
145 150 155 160  
Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg  
165 170 175  
Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu  
180 185 190  
Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys  
195 200 205  
Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val  
210 215 220  
Leu Trp Ser Asp Gly Asp Gly Ala Pro Asp Gln Tyr Trp Asn Ser  
225 230 235 240  
Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr  
245 250 255  
Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly  
260 265 270  
Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro  
275 280 285  
His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr  
290 295 300  
Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val  
305 310 315 320  
Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Met Asn  
325 330 335

35/177

Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg  
340 345 350  
Leu Arg Glu Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
355 360 365  
5 Glu Thr His Thr Arg Ser Glu Asn Asp Thr Val Thr Pro Asp Val  
370 375 380  
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
385 390 395 400  
Lys Trp Pro Thr Ser Gly Glu Leu Phe Leu Gly His Pro Lys Ala Ile  
405 410 415  
10 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Glu Pro Leu Asn  
420 425 430  
Trp Ile Ser Leu Glu Glu Asn Gly Ile Met Val Glu Leu Pro Glu Leu  
435 440 445  
15 Thr Ile His Glu Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
450 455 460  
Asn Val Ile  
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20 <210> 34  
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25 <400> 34  
Met Asp Asn Val Glu Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser  
1 5 10 15  
Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu  
20 25 30  
30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro  
35 40 45  
Glu Thr Thr Thr Leu Thr Val Gly Gly Val Val Phe Ala Leu Val Thr  
50 55 60  
Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu  
65 70 75 80

36/177

Phe Asn Pro Ser Gly Pro Tyr Glu Glu Lys Pro Val His Glu Lys Lys  
85 90 95  
Glu Val Leu  
5 <210> 35  
<211> 189  
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<213> Homo sapiens  
10 <400> 35  
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1 5 10 15  
Leu Val Leu Ser Gly Ala Trp Gly Met Glu Met Trp Val Thr Phe Val  
20 25 30  
15 Ser Gly Phe Leu Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu  
35 40 45  
Val Glu Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys  
50 55 60  
Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Glu His Ala Trp Ala Glu  
65 70 75 80  
Leu Thr Phe Trp Glu Ala Ser Glu Leu Tyr Leu Leu Phe Leu Ser Leu  
85 90 95  
Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Glu Pro Arg Thr Thr Ala  
100 105 110  
25 Ala Met Trp Ala Leu Glu Thr Val Glu Lys Glu Arg Gly Leu Gly Gly  
115 120 125  
Glu Val Pro Gly Ser His Glu Gly Pro Asp Pro Tyr Arg Glu Leu Arg  
130 135 140  
30 Glu Lys Asp Pro Lys Tyr Ser Ala Leu Arg Glu Asn Phe Phe Arg Tyr  
145 150 155 160  
His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly  
165 170 175  
Leu Cys Leu Ala Gly Leu Ala Leu Glu Ile Arg Ser Leu  
180 185

37/177

38/177

&lt;210&gt; 36

&lt;211&gt; 363

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

5

&lt;400&gt; 36

Met Val Asp Ser Leu Leu Ala Val Thr Leu Ala Gly Asn Leu Gly Leu

1

5

10

15

Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr

10

20

25

30

Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu

35

40

45

Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu

50

55

60

Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Gln Pro Arg

65

70

75

80

Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala

85

90

95

Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala

100

105

110

Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val

115

120

125

Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Cys Met Ser

130

135

140

Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr

145

150

155

160

Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly

165

170

175

Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly

180

185

190

Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp

195

200

205

Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln

210

215

220

Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

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39/177

85 90 95  
Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val Ala Asn Lys Ile  
100 105 110  
Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu Asn Ala Leu Asn  
5 115 120 125  
Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val  
130 135 140  
Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly  
145 150 155 160  
10 Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser Leu Tyr Asp Ser  
165 170 175  
His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn  
180 185 190  
Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr  
15 195 200 205  
Phe Thr Glu Gly Ser Leu Phe Leu Leu His Gly Glu Cys Ala  
210 215 220  
Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala Glu Val Lys Glu  
225 230 235 240  
20 Lys Val Val Thr Ile Ile Pro Lys Ile  
245  
<210> 38  
<211> 98  
<212> PRT  
25 <213> Homo sapiens  
<400> 38  
Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile  
30 1 5 10 15  
Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe  
20 25 30  
Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu  
35 35 40 45  
Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln

40/177

50 55 60  
Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Gly  
65 70 75 80  
Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met  
5 85 90 95  
Val Arg  
<210> 39  
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<212> PRT  
10 <213> Homo sapiens  
<400> 39  
Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu  
15 1 5 10 15  
Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly  
20 25 30  
Gln Thr Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr  
35 40 45  
20 Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile  
50 55 60  
Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu  
65 70 75 80  
Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser  
25 85 90 95  
Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His  
100 105 110  
Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val  
30 115 120 125  
Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala  
130 135 140  
Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro  
145 150 155 160  
35 Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe  
165 170

42/177

**<213> Homo sapiens**

30 tttgaagata agagggaaag tagaact

**<210> 43**

**<211> 1401**

**<212> DNA**

**<213> Homo sapiens**

43/177

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ctcgagccgag cgcgcgtgcgc tgcgcacagc gcccagcgct tcgaacccac ctggagctcc	120
ctggagccgc gcccagctgcgc cgcgtcgttt gaccagggca agttcgacat cttaacacac	180
tggggagctgt ttcccgctgcgc cagcttcggt agcgagctgtt tctgttggtg ttggcaaaag	240
gaaaagatac cgaagctatgt ggaattatcg aaagataatt accctcctcg tttaaatat	300
gaagattttg gaccacatit tacagcaaaa ttittaatg ccacacagtg ggcagatatt	360
ttcagggcct ctggtgcgca ataatctgtc tttaatcga aacatcatga agctttacc	420
ttgttgggggt cagaatattc gtggagcttg aatgcatag atggaggggc caagggggagc	480
attgtcaag agacttgaggt agccatlagg aacagagctg acctcgcttt tggactgtac	540
tattcccttt ttgaatgggt tcatccgctc ttccctggag atgaatccag ttcatctcat	600
aagcggcaat ttccagtttc taagacatlg ccagagctct atgagttagt gaaacaatat	660
cagcctgaggt ttctgtgtgc ggaatgtgac ggaagggcac cggatcaata ctggaaacagc	720
aaagctctct tggcctgggt ataatagaa agccagctc gggggacagt agtacaatat	780
gactgtggg gaggctgtgag catctgtaag calgtgtggt tctataacct cagtgtacgt	840
tataaccaa gacatcttt gccacataa tgggaaacct gcatgacaat agacaacctg	900
tctgtgggtc ataggaggga agcttgaaac tctgactac ttacaatga agaatgtgtg	960
aaagaaacttg taagaagact ttcatgtgga ggaatcttt tgaatgaat tgggcacaca	1020
ctagatggca ccaattctgt agttttgag gagcgactga ggaatgggg gtccctggcta	1080
aaagtaatg gagaagctat ttatgaacc catnctggc gatccagaa tgaactgtc	1140
accagagatg tgtgtacac atccagact aaagaaatat taqtatagc caattttct	1200
aaatggccca catcagagca gctgttcctt ggcacccca aagtatctt gggggcaaca	1260
gagctgaac tactgggcca tggagagca cttaactgga ttctcttga gcaaatgggc	1320
attatgtgag aactgcacaa gctaaccaat catagatgc cgtgtaaatg gggctgggt	1380
ctagccctga ctatctgt c	1401
<210> 44	
<211> 297	
<212> DNA	
<213> Homo sapiens	
<400> 44	
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gtgaagatgc tggcgttga tattatcaac tcaatgtaa caacagatatt catgtcatc	120

44/177

gtatctgtgt tgcagactgat accagaaacc acaacatga caattgtgtg aggggtcttt	180
gaactgtga cagagtatag ctgtcttgcg gacggggccc ttattaccg gaactctcig	240
ttcaatccca ggggtacctta ccaagaaag ccgtgtcatg aaaaaaaga agttttg	297
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ggtgcctggg gaatgaaat gtgggtgacg ttgcctoaag gcttccatgt ttccgaagc	120
cttcccgac ataccttgg actagtgag agcaaatctc tcccttcta ctccaacac	180
tcaatgggt gtgccttat caacctcgc atcttgctt ccaagcatgc ttggctcag	240
ctcaaatct gggagggcag ccagcttaac ctgccttcc tgaacttaac gctggcact	300
gtcaagccc gctgtctgga accccgacac aaagctgcca tgttggccct gcaaacggtg	360
ggaagggagc gaggcctggg tggggagta ccagggagc accaggttcc cgaatccac	420
cgcagactgc gagaagagga ccccaagtac agtgcctcc gccagaaatt ctccgctac	480
catgggtgt cctctcttg caatctggc tggctcttga gaaatgggt ctgtctcgt	540
ggccttgcgc tggaaataag gggcctc	567
<210> 46	
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<400> 46	
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ggttcccaaa ccaagagcca tccagactg ggaactgag gctgttggga ccaagctatc	120
ggcccttga cctttacgt ttggacccc aaggaatcc tgttaaccaa ggccttccctc	180
aatgggccc tgaatgggtt catcttga gactactga gccggactcc tgaacccgg	240
ccatccctca gcaacttgc ggcagatgc tatgggctg ggttggccag agacccaggg	300
ttccgagca acttccagc ggaagaggt gctgtctga cttaagctc catcttggc	360
cagaggtgtt ggggaacct tptcttcta cagaagcttg agcagatca cctcaagctt	420
caatgtatga gcaagaaaca gcttggccag gttgttgcga atgtatacaa ggaattcatc	480

45/177

46/177

gagggcttcc tggggtgccc ggcacacac ccccgctgcc gctggggagc ggcgcttat 540  
cggggcgccc cgaagtgtgt gacgtgccg ctggggattct tgaagtga taacacctac 600  
gtgctgacac caccctgccc gaccttcacg cgtgcgcag ccaacatgcg ctccatgcag 660  
cgtacacccc agaacacgca aggtctgggga gaacatgctt acagtttctgt ggtggctgcg 720  
gacggttacg tgaacgaggg acgcgcttgc cactgggttg gacgacacac gctcgccac 780  
aacctccggg gcttcggcgt ggcacatgty ggcacacac cgcggcgct gccacacgag 840  
gcccctctgc gacgggtgcg gacacacgc cagagttgtg cgggtgcgcgc cggctctctg 900  
cggcgagact acgctgtgt cagtcacacg cagctggtgc gacggactg ccccgcgac 960  
gcgtcttcg acgtgtgcg cactggcgcc cactcacccg cgaatgttaa gcaagaacct 1020  
gccaggagtg tctctaaag atccaggagg gacgcacccc caaggacct gccagccaca 1080  
gacctccaa 1089

&lt;210&gt; 47

&lt;211&gt; 747

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

atgggtggcc cccggggcgc gggctgggtg gcggcgggcc tgcgtctcg cggggcgccc 60  
tgaactgca ttacaggct gaccgggggt cggcgcgggg ggcagcgca gctcgggata 120  
cgtctctcga agtcgcgaga agacttaact gatgggttcat atgatgatgt tctaatgct 180  
gaacacctic agaaactct ttacctgctg gagtcacagg aggtacctgt aattattgaa 240  
agaacttga ttactttggg taacaatgca gcccttttcag ttacccaagc tattattcgt 300  
gaattgggtg gtattccaat tgttgaac aaaaacaacc attccaacca gagtattaaa 360  
gagaaagctt taatgcaact aaataacctg agtgtgaatg ttgaataca aatcaagata 420  
aaggtgcaag ttctgaact gcttttgaat ttgtctgaaa atcccgccat gacagaaggga 480  
cttctccgtg cccaagtga ttacatctt ctttcccttt atgacggcca cgtagcaaaag 540  
gagatcttic ttgagtgact taagctattt cagaaataaa agaaactgct caaaatagaa 600  
ggccatttag ctgtgcagcc tacttcaact gaaggttcat tgttttctt gttacatgga 660  
gaagaatgtg ccagaaaat agaggtctta gtgatccacc atgatgcaga ggtgaaggaa 720  
aaggttgtaa caataatccc caaatac 747

&lt;210&gt; 48

&lt;211&gt; 294

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

atggctgcg tccgtgtgct tgggcgaag ctggcgccct gggcctagt cctcagcgcc 60  
tggggagiga tcatgttgat aatgctcga atattttca atgtccatc cgtgtgttg 120  
attgagcag ttccctcac ggcgaagat tttagaatg gcccccgaa catataaac 180  
cttaccgagc aagtacgcta caactgttc atcgtgcag gctttacct cctctcaga 240  
ggttctatt ttgcgaagt tggctcaat aagcgcaag aatacatggt gcgc 294

10 &lt;210&gt; 49

&lt;211&gt; 516

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

15 &lt;400&gt; 49

atggtggccc ccgcgcgcg gcggcgctg cggccgctgg cagcgctggc cctgtctctg 60  
gcgtggccc cggggctgcc caccgcggg gcggggcaga caccgcgcc tgcgagcgg 120  
gggcccacg tgcgctttt caccggggag gagctggccc gctatggcg ggaaggggaa 180  
gacagccca tctactggc agtgaaggga gtgggtgttg atgtcacctc cggaaaggag 240  
ttttatgac gagggagccc ctacaatgcc ttgacgggga aggaactcac tagaggggta 300  
gccaagatgt cctggatcc tgcagacctc acccatgaca ctacgggtct cagggccaag 360  
gaactggagg ccttgatga ggtcttacc aaagtgtaca aagcaataa ccccatctc 420  
ggctacatg ccggagaaat tctcaatgag gatggcagcc ctacactgga ctteagacct 480  
gaagaccagc cccattttga catcaaggat gagtgc 516

25 &lt;210&gt; 50

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

30 &lt;400&gt; 50

atgatgcct cccgtaccca cctggctact ggaatccca gtagtaagt gaatatctca 60  
aggctctca gcaagacga tggctacatt gacctcagt ttaagaaac cctctctag 120  
atccctata aggcacgcg acttgcaact gtgtgtttt tgattggcg cttctctatt 180  
attatagct cctctctgct gtcaggctac atcagcaag gggggcgaga ccggcgctt 240

47/177

ccagtgctga tcaatggat tctgtgttc ctaccggat ttaccacc ggcgctgc 300  
tactatgat ccaagagcta ccgtgttacc tccatgatg acattccaga cttgatgac 360

<210> 51  
<211> 1065  
<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS  
<222> (2)...(943)

<400> 51  
a atg aac caa ctc agc ttc ctg ctg ttc ctg ata gag acc acc aga gga 49  
Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly  
1 5 10 15  
tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97  
Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
20 25 30  
tcg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145  
Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
35 40 45  
cct agt gca ttt gat ggc ctg tat ttt ctg cgc act gag aat ggt gtc 193  
Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
50 55 60  
atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241  
Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Trp Thr  
65 70 75 80  
ctg gtg ggc agc gtc cat gag aat gac atg cgt ggg aag tgc aag gtc 289  
Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
85 90 95  
ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 317  
Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu  
100 105 110  
ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag ggc 385  
Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala

48/177

ggc aag agc gat gac tac aag aac cct ggc tac tac gac atc cag gcc 433  
Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala  
115 120 125  
130 135 140  
aag gac ctg ggc atc tgg cgc gtc ccc aat aag tcc ccc atg cag cac 481  
Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His  
145 150 155 160  
tgg aga aac agc tcc ctg ctg agg tac cgc aag gac act ggc ttc ctg 529  
Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu  
165 170 175  
cag aca ctg gga cat aat ctg ttt ggc atc tac cag aaa tat cca gtc 577  
Gln Thr Leu Gly His Asn Leu Phe Phe Ile Tyr Gln Lys Tyr Pro Val  
180 185 190  
aaa tac gga gaa gga aag tgt tgg act gac aac ggc ccg gtc atc cct 625  
Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro  
195 200 205  
gtg gtc tat gat ttt ggc gac gcc cag aaa aca gaa tct tat tac tca 673  
Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser  
210 215 220  
ccc tat ggc cag cgg gaa ttc act gcg gga ttt gtc cag ttc aag gta 721  
Pro Tyr Gly Gln Arg Glu Glu Phe Thr Ala Gly Phe Val Phe Arg Val  
225 230 235 240  
ttt aat aac gag aga gca gcc aac gcc ttg tgc gct gga atg aag gtc 769  
Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val  
245 250 255  
acc gga tgt aac aat gag cac cac tgc att ggt gga gga gaa tac ttt 817  
Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe  
260 265 270  
cca gag ggc agt ccc cag cag tgt gga gat ttt tct ggt ttt gat tgg 865  
Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp  
275 280 285  
agt gga tat gga act cat gtt ggt tac agc agc agc cgt gag ata act 913  
Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr  
290 295 300  
gag gca gct gtc ctt cta ttc tct cgt tgaaggtttt gtggagggga 960

49/177

50/177

Glu Ala Ala Val Leu Leu Phe Tyr Arg

305 310  
 accagaccct ctctctccaa ccatgagatc ccaaggatgg agaaacatt accacgtage 1020  
 tagaatgta atggcgag agaaacaat aaatcatatt gactc 1065

6

&lt;210&gt; 52

&lt;211&gt; 937

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

10 &lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (177)...(866)

&lt;400&gt; 52

15 cttttggaga actgagcttc tctttggag ggaagtgtcg cagcgcgcc ggcgcacac 60  
 tggagtttct tcaagactcca gatttccctg tcaaccaga ggaagtcaga gaggaanagc 120  
 ggaagggaga caacagtaacc tgacgcctat ttaagccgg gatgcaccca gaaggg 176  
 atg ggc gac aag atc tgg ctg ccc ttc ccc gtg etc ctt ctg gcc get 224  
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Ala Ala

20

1 5

10

15

ctg cct ccg gtg ctg cct ggg gcg gcc ggc ttc aca cct tcc etc 272  
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu

gat agc gac ttc acc ttt acc ctt gcc gcc gcc agc gag tgc ttc 320  
 Asp Ser Asp Phe Thr Phe Thr Leu Leu Pro Ala Gly Gln Lys Glu Cys Phe

35 40 45  
 tac aag ccc atg ccc ctg aag gcc teg ctg gag atc gag tac caa gtt 368  
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val

25 20 25 30  
 tta gat gga gca tta gat att gat ttc cat ctt gcc tct cca gaa 416  
 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

65 70 75 80  
 ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act 464  
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr

35

85

90

95

gta gag act gaa gtt ggt gat tac atg ttc tgc ttt gac aat aca ttc 512  
 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe  
 100 105 110  
 agc acc att tct gag aag gtg att ttc ttt gaa tta atc ctg gat aat 560  
 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn

5

115

120

125

atg gga gaa cag gca caa gaa gat tgg aag aaa tat att act 608  
 Met Gly Glu Gln Ala Gln Glu Asp Trp Lys Lys Tyr Ile Thr

130

135

140

ggc aca gat ata ttg gat atg aaa ctg gaa gac atc ctg gaa tcc atc 656  
 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile

10

145

150

155

aac agc atc aag tcc aga cta agc aaa agt ggg cac ata caa att ctg 704  
 Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu

165

170

175

ctt aga gaa ttt gaa get cgt gat cga aac ata caa gaa agc aac ttt 752  
 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe

180

185

190

gat aga gtc aat ttc tgg tct atg gtt aat tta gtg gtc atg gtg gtg 800  
 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val

15

195

200

205

gtg tea gcc att caa gtt tat atg ctg aag agt ctg ttt gaa gat aag 848  
 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys

210

215

220

agg aaa agt aga act taaactcca aactagagta cgtacattg aaaaatg 900  
 Arg Lys Ser Arg Thr

25

225

230

235

aggcataaaa atgcataaaa ctgttacagt cangacc 937

30

&lt;210&gt; 53

&lt;211&gt; 1678

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

51/177

<2222> (56) ... (1459)

5	atg cgg ccc cag gag ctc ccc aag ctc gcg ttc cgg tgg ctg ctg tgg	103
10	Met Arg Pro Gln Gln Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	
15	ctg ttg ctg ctg ctg ccg ccg ccg tgc cct gcc cac aag gcc aag	151
20	Leu Leu Leu Leu Leu Pro Pro Cys Pro Ala His Ser Ala Thr	
25	cgc ttc gac ccc acc tgg gag tcc ctg gac gcc cgc cag ctg ccc gcg	199
30	Arg Phe Asp Pro Thr Trp Gln Ser Leu Asp Ala Arg Gln Leu Pro Ala	
35	tgg ttt gac cag gcc aag ttc ggc atc ttc acg cag tgg gga gtg ttt	247
40	Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	
45	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag	295
50	Ser Val Pro Ser Phe Gly Ser Gln Trp Phe Trp Tyr Trp Gln Lys	
55	gaa aag ata ccg aag tat gtg gaa ttt atg aaa gat aat tac cct cct	343
60	Gln Lys Ile Pro Lys Tyr Val Gln Phe Met Lys Asp Asn Tyr Pro Pro	
65	agt ttc aaa tat gaa gat ttt gga cca cta ttt acca gca aaa ttt ttt	391
70	Ser Phe Lys Tyr Gln Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	
75	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac	439
80	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	
85	att gtc tta act tcc aaa cat cat gaa gcc ttt acc ttg tgg ggg tca	487
90	Ile Val Leu Thr Ser Lys His His Gln Gly Phe Thr Leu Trp Gly Ser	
95	gaa tat tgg tgg aac tgg aat gcc ata gat gag ggg ccc aag aag gac	535
100	Gln Tyr Ser Trp Asn Trp Asn Ala Ile Asp Gln Gly Pro Lys Arg Asp	
105	att gtc aag gaa ctt gag gta gcc att aag aac aga act gac ctg cgt	583

521177

	165	170	175	
Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg				
ttt gga ctg tac tat tcc cct ttt gaa tgg ttg cat ccg ctg ttc ctt				631
Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu				
180	185	190		
gag gat gaa tcc agt tca ttc cat aag ccg caa ttt coa gtt tct aag				679
Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys				
195	200	205		
aca ttg cca gag ctg tat gag tta gtg aac aac tat cag cct gag gtt				727
Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val				
210	215	220		
ctg tgg tcg gat ggt gac gga gga gca ccg gat caa tac tgg aac agc				775
Leu Trp Ser Asp Gly Asp Gly Ala Pro Asp Gln Tyr Trp Asn Ser				
225	230	235	240	
aca ggc ttc ttg gcc tgg tta tat aat gaa agc cca gtt ccg ggc aca				823
Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr				
245	250	255		
gta gtc acc aat gat cgt tgg gga gct ggt agc atc tgt aag cat ggt				871
Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly				
260	265	270		
ggc ttc tat acc tgc agt gat cgt tat aac cca gga cat ctt ttg cca				919
Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro				
275	280	285		
cat aaa tgg gaa aac tgc atg aca ata gac aaa ctg tcc tgg ggc tat				967
His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr				
290	295	300		
agg agg gaa gct gga atc tct gac tat ctt aca att gaa gaa ttg gtg				-1015
Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val				
305	310	315	320	
aag caa ctt gta gag aca gtt tcatgt gga gga aat ctt ttg atg aat				1063
Lys Glu Leu Val Glu Thr Val Ser Cys Gly Asn Leu Leu Met Asn				
325	330	335		
att ggg ccc aca cta gat ggc acc att tct gta gtt ctt gag gag cga				1111
Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg				
340	345	350		

53/177

54/177

ctg agg caa atg ggg tcc tgg cta aaa gtc aat gga gaa gct att tat 1159  
Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr 365  
355  
gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat gtg 1207  
Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Trp Pro Asp Val 380  
370 375  
tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ott 1255  
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu 400  
385 390 395  
aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att 1303  
Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile 415  
405 410  
ctg ggg gca aca gag gtg aca cta ctg ggc cat gga cag cca ctt aac 1351  
Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn 430  
425  
tgg att tct ttg gag caa aat ggc att atg gta gaa ctg cca cag cta 1399  
Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu 445  
435 440  
acc att cat cag atg ccg tgt aat tgg ggc tgg gct cta gcc ctg act 1447  
Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr 460  
450 455  
aat gtg atc taaagtgcag cagagtggct gatgtgcaa gttatgcta aggc 1500  
Asn Val Ile 465  
taggaactat caggtgtcta taattgagc acatggagaa agcaaatgta aaactggata 1560  
agaaattat ttggagtt cagcccttcc ccttttccc actaaatttt ttctaaatt 1620  
accatgaa ccattttaac tctccagtcg acttggccat taaagtctct tcaacttg 1678

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<212> DNA  
<213> Homo sapiens  
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<221> CDS  
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cagccagctg agaagagttg agggaaagtg ctgctgtcgg gtctgcagac ggc atg 116  
Met  
gat aac gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg 1  
Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val  
5 10 15  
aaa ggc cac gtg aag atg ctg cgg ctg gat att atc aac tca ctg gta 212  
Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu Val  
20 25 30  
aca aca gta ttc atg ctc atc gta tct gtg ttg gca ctg ata cca gaa 260  
Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Glu  
35 40 45  
acc aca aca ttg aca gtt ggt gga ggg gtg ttt gca ctt gtg aca gca 308  
Thr Thr Leu Thr Val Gly Gly Val Phe Ala Leu Val Thr Ala  
50 55 60  
gta tgc tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc 356  
Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe  
70 75 80  
aat ccc agc ggt cct tac cag caa aag cct gtg cat gaa aaa aaa gaa 404  
Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys Glu  
85 90 95  
gtt ttg taattttata ttacttttta gtttgtact aagtattaaa 450  
Val Leu  
catattctcg tattctt 467

<210> 55  
<211> 875  
<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS



55/177

&lt;222&gt; (272)...(841)

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gggtgtctcg gattgagct ccggtctcta acgactctc gtctgatttg ccgttaacct 180  
gtcccgagac gggctcacag ggtctgaag ccaagcatga ggaagatga aagttctgag 240  
ccaaccgttg cctcctctcc aggaactgaa g atg gag gaa ggc ggg aac cta 292  
Met Glu Glu Gly Gly Asn Leu  
1 5  
gga ggc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt ggc tgg 340  
Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp  
10 15 20  
ggc atg caa atg tgg gtc acc ttc gtc tca ggc ttc ctg ctc ttc cga 388  
Gly Met Glu Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg  
25 30 35  
agc ctt ccc cga cat acc ttc gga cta gtc cag ago aaa ctc ttc ccc 436  
Ser Leu Pro Arg His Thr Phe Gly Leu Val Glu Ser Lys Leu Phe Pro  
40 45 50 55  
ttc tac ttc cac atc tcc atg ggc tgt gcc ttc atc aac ctc tgc atc 484  
Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile  
60 65 70  
ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc 532  
Leu Ala Ser Glu His Ala Trp Ala Glu Leu Thr Phe Trp Glu Ala Ser  
75 80 85  
cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc acc gtc aac ggc 580  
Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala  
90 95 100  
cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc 628  
Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Glu Thr  
105 110 115  
gtg gag aag gag cga ggc ctg ggt ggg gag gta cca ggc agc cag 676  
Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Glu  
120 125 130 135  
ggt ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt 724

56/177

Gly Pro Asp Pro Tyr Arg Glu Leu Arg Glu Lys Asp Pro Lys Tyr Ser  
140 145 150  
gct ctc cgc cag aat ttc ttc cgc tac cat gag ctg tcc tct ctc tgc 772  
Ala Leu Arg Glu Asn Phe Arg Tyr His Gly Leu Ser Ser Leu Cys  
155 160 165  
aat ctg ggc tgc gtc ctg agc aat ggg ctc tgt ctc gct ggc ctc gcc 820  
Asn Leu Gly Cys Val Leu Ser Asn Gly Leu Cys Leu Ala Gly Leu Ala  
170 175 180  
ctg gaa ata agg agc ctc tagcatggc cctgcattgt aataatgct tcttcag 875  
Leu Glu Ile Arg Ser Leu  
185  
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<222> (150)...(1241)  
<400> 56  
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atattgagc caaactctca gatgtacaa aaggctgtcc agatgtccaa gttccttgc 120  
cagatgcac agccaagtcc ccaaccgacc atg gtc gag agc ctc ctg gca gtc 173  
Met Val Asp Ser Leu Leu Ala Val  
1 5  
aac ctg gct gga aac ctg ggc ctg acc ttc ctc cga ggt tcc cag acc 221  
Thr Leu Ala Gly Asn Leu Gly Leu Thr Phe Leu Arg Gly Ser Glu Thr  
10 15 20  
cag agc cat cca gac ctg gga act gag ggc tgc tgg gac cag ctc tct 269  
Gln Ser His Pro Asp Leu Gly Thr Glu Gly Cys Trp Asp Glu Leu Ser  
25 30 35 40  
gcc cct cgg acc ttc acg ctt ttg gac ccc aag gca tct ctg tta acc 317  
Ala Pro Arg Thr Phe Thr Leu Leu Asp Pro Lys Ala Ser Leu Leu Thr  
45 50 55

57/177

58/177

aag gcc ttc ctc aat ggc gcc ctg gat ggg gtc atc ctt gga gac tac 365  
 Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr 70  
 60 65  
 ctg agc egg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc 413  
 Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser 85  
 75 80  
 cag tac tat ggg gct ggg gtc gcc aga gac cca ggg ttc cgc agc aac 461  
 Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn 100  
 90 95  
 ttc cga cgg cag aac ggt gct ctg act tca gcc tcc atc ctg gcc 509  
 Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala 115  
 105 110  
 cag cag gtc tgg gga acc ctt gtc ctt cta cag agg ctg gag cca gta 557  
 Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val 135  
 125 130  
 cac ctc cag ctt cag tgc atg agc caa gaa cag ctg gcc cag gtc gct 605  
 His Leu Gln Leu Gln Cys Met Ser Gln Gln Gln Leu Ala Gln Val Ala 150  
 140 145  
 gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc ccg gcc 653  
 Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala 165  
 155 160  
 atc cac ccc cgc tgc cgc tgg gga ggc ggc cct tat cgg ggc cgc ccg 701  
 Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro 180  
 170 175  
 aag ctg ctg cag ctg ccg ctg gga ttc ttg tac gtc cat cac acc tac 749  
 Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr 195  
 185 190  
 gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg 797  
 Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met 215  
 205 210  
 cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc 845  
 Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile 230  
 220 225  
 ggc tac agt ttc gtc gtc ggc tgc gac gcc tac gtc tac gag gga cgc 893  
 Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg 245

235 240 245  
 ggc tgg cac tgg gtc ggc gcc cac acg ctc ggc cac aac tcc cgg ggc 941  
 Gly Trp His Trp Val Gly Ala His Thr Leu Gly His Asn Ser Arg Gly 255 260  
 250  
 5 ttc ggc gtc gcc ata gtc ggc aac tac acc ggc ggc ctg ccc acc gag 999  
 Phe Gly Val Ala Ile Val Gly Asn Tyr Thr Ala Ala Leu Pro Thr Glu 275 280  
 265 270  
 gcc gct ctg cgc acg gtc ggc gac acg ctc ccc agt tgc ggc gtc cgc 1037  
 Ala Ala Leu Arg Thr Val Arg Asp Thr Leu Pro Ser Cys Ala Val Arg 295  
 285 290  
 10 gcc ggc ctc ctg cgg cca gac tac ggc ctg ctg ggc cac cgc cag ctg 1085  
 Ala Gly Leu Leu Arg Pro Asp Tyr Ala Leu Leu Gly His Arg Gln Leu 310  
 300 305  
 15 gtg cgc acc gac tgc ccc ggc gac ggc ctg ttc gac ctg ctg cgc acc 1133  
 Val Arg Thr Asp Cys Pro Gly Asp Ala Leu Phe Asp Leu Leu Arg Thr 325  
 315 320  
 tgg ccg cac ttc acc ggc act gtt aag cca aga cct gcc agg agt gtc 1181  
 Trp Pro His Phe Thr Ala Thr Val Lys Pro Arg Pro Ala Arg Ser Val 340  
 330 335  
 20 tct aag aga tcc agg agg gag cca ccc cca agg acc ctg cca gcc aca 1229  
 Ser Lys Arg Ser Arg Arg Glu Pro Pro Pro Arg Thr Leu Pro Ala Thr 355 360  
 345 350  
 gac ctc caa taagacagc atggaaac 1256  
 Asp Leu Gln  
 25 <210> 57  
 <211> 884  
 <212> DNA  
 <213> Homo sapiens  
 30 <220>  
 <221> CDS  
 <222> (135)...(884)  
 35 <400> 57  
 cattctctt ctcacatcc aggtcaggtg ggcgttgcg tggcggctag gccgcgtgc 60

69/177

gacgagagac tccgcctctg ccccccgcag cctctctgcc tggccgcgcg ctgcgctctc 120  
gcccgcgcgcg aagc atg ggt ggc ccc cgg ggc ggc tgg gtc ggc ggc 170  
Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala  
1 5 10  
5 ggc ctg ctg ctg ggc ggc ggc tgc tac tgc att tac aag ctg acc 218  
Gly Leu Leu Leu Gly Ala Gly Ala Cys Tyr Ile Tyr Arg Leu Thr  
15 20 25  
cgg ggt cgg cgg ggc ggc ggc cgc gag ctg ggg ata cgc tct tcc aag 266  
Arg Gly Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys  
30 35 40  
10 tcc gca gaa gac tta act gat gat tca tat gat gat gtc cta aat gct 314  
Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala  
45 50 55 60  
gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct 362  
Glu Glu Leu Glu Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro  
65 70 75  
15 gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt 410  
Val Ile Ile Glu Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Phe  
80 85 90  
20 tca gtt aac caa gct att att cgt gaa ttg ggt ggt att cca att gtt 458  
Ser Val Asn Glu Ala Ile Ile Arg Glu Leu Gly Ile Pro Ile Val  
95 100 105  
gca aac aaa atc aac cat tcc aac cag agt att aaa gag aaa gct tta 506  
Ala Asn Lys Ile Asn His Ser Asn Glu Ser Ile Lys Glu Lys Ala Leu  
110 115 120  
25 aat gca cta aat aac ctg agt gtc aat gtt gaa aat caa atc aag ata 554  
Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Glu Ile Lys Ile  
125 130 135 140  
aag gtc caa gtt ttg aaa ctg ctt ttg aat ttg tct gaa aat cca gcc 602  
Lys Val Glu Val Leu Lys Leu Leu Asn Leu Ser Glu Asn Pro Ala  
145 150 155  
30 atg aca gaa gga ctt ctc cgt gcc caa gtc gat tca tca ttc ctt tcc 650  
Met Thr Glu Gly Leu Leu Arg Ala Glu Val Asp Ser Ser Phe Leu Ser  
160 165 170  
35 ctt tat gac agc cac gta gaa aag gag att ctt cga gta ctt acg 698

60/177

Leu Tyr Asp Ser His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr  
175 180 185  
cta ttt cag aat ata aag aac tgc ctg ctc aaa ata gaa ggc cat tta gct 746  
Leu Phe Glu Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala  
190 195 200  
5 gtc aag cct act ttc act gaa ggt tca ttg ttt ttc ctg tta cat gga 794  
Val Glu Pro Thr Phe Thr Glu Gly Ser Leu Phe Leu Leu His Gly  
205 210 215 220  
10 gaa gaa tgt gcc cag aaa ata aga gct tta gtt gat ccc cat gat gca 842  
Glu Glu Cys Ala Glu Lys Ile Arg Ala Leu Val Asp His His Asp Ala  
225 230 235  
gag gtc aag gaa aag gtt gta aca ata cca aaa atc tga 884  
Glu Val Lys Glu Lys Val Val Thr Ile Ile Pro Lys Ile  
240 245  
15 <210> 58  
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<400> 58  
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Met Ala Ser  
1  
ctc ctg tgc tgt ggg cag aag ctg gcc tgc ggc atc gtc ctc agc 104  
Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser  
5 10 15  
30 gcc tgg gga gtc atc atg ctg ata atg ctg gga ata ttt ttc aat gtc 152  
Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val  
20 25 30 35  
cat tcc gct gtc ttg att gag gac gtc ccc ttc acg gag aaa gat ttt 200  
His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu Lys Asp Phe

61/177

62/177

40 45 50  
gag aat ggc ccc cag aac ata tac aac att tac gag caa gtc agc tac 248  
Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr  
55 60 65  
aac tgt ttc atc gct gca ggc att tac etc etc etc gga ggc ttc tct 296  
Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser  
70 75 80  
ttc tgc caa gtt cgg etc aat aag cgc aag gaa tac atg gtg cgc 341  
Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg  
85 90 95  
tagggccc ggcgcgttc cccgcctccag cccctctct atttaagac tccctgcacc 400  
gtgtacacca ggtcgcgtcc caccctggc ggcgcctct gtggacttg gttcccggg 460  
cgagactg aatccctct cccatctctg gcaccggcc cccgtggaga gggctgggc 520  
tggggggtg ttcgtctct cccaccttg ctgtgtccg tatcacaata aaggaatct 580  
gtctcttc 589  
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<400> 59  
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Met Val Gly Pro Ala Pro Arg Arg  
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ctg cgg ccg ctg gca ggc ctg gcc ctg gtc ctg ggc ctg gcc cgg ggg 99  
Leu Arg Pro Leu Ala Ala Leu Ala Leu Val Leu Leu Ala Leu Pro Gly  
10 15 20 25  
ctg ccc aca gcc cgg gcc ggg cag aca ccg cgc cct gcc gag cgg ggg 147  
Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly  
30 35 40  
ccc cca gtg cgg ctt ttc acc gag gag gag ctg gcc cgc tat gcc ggg 195

Pro Pro Val Arg Leu Phe Thr Glu Glu Leu Ala Arg Tyr Gly Gly 55  
45 50  
gag gag gaa gat cag ccc atc tac ttg gca gtg aag gga gtg gtg ttt 243  
Glu Glu Glu Asp Gln Pro Ile Tyr Leu Ala Val Lys Gly Val Val Phe  
60 65 70  
gat gtc acc tcc gga aag gag ttt tat gga cga gga gcc ccc tac aat 291  
Asp Val Thr Ser Gly Lys Glu Phe Tyr Gly Arg Gly Ala Pro Tyr Asn  
75 80 85  
gcc ttg acg ggg aag gac tcc act aga ggg gta gcc aag atg tcc ttg 339  
Ala Leu Thr Gly Lys Asp Ser Thr Arg Gly Val Ala Lys Met Ser Leu  
90 95 100 105  
gat cct gca gac etc acc cat gac act ggc ggt etc acg gcc aag gaa 387  
Asp Pro Ala Asp Leu Thr His Asp Thr Thr Gly Leu Thr Ala Lys Glu  
110 115 120  
ctg gag gcc ctg gat gag gtc ttc acc aca gta gcc aca gcc aca tac 435  
Leu Glu Ala Leu Asp Glu Val Phe Thr Lys Val Tyr Lys Ala Lys Tyr  
125 130 135  
ccc atc gtc ggc tac act gcc cgg aga att ctc aat gag gat ggc agc 483  
Pro Ile Val Gly Tyr Thr Ala Arg Arg Ile Leu Asn Glu Asp Gly Ser  
140 145 150  
cct aac ctg gcc ttc aag cct gaa gac cag ccc cat ttt gac atc aag 531  
Pro Asn Leu Asp Phe Lys Pro Glu Asp Gln Pro His Phe Asp Ile Lys  
155 160 165  
gat gag ttc tgatgtccc cctgcaggag caggctcttg ggcgcgtgag 580  
Asp Glu Phe  
170  
gcaggagac actaggtgct gaatctctg caaaactggc tgctggagg cctgagccc 640  
ccagatctg aataaacag atgcttaacc tgg 673

63/177

&lt;222&gt; (127)...(489)

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 cgtgct atg atg cgg tcc cgt acc aac ctg gct act gga atc ccc agt 168  
 Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser  
 1 5 10  
 agt aac gtg aaa tat tca agg ctg tcc agc aca gac gat ggc tac att 216  
 Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile  
 15 20 25 30  
 gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gac atc 264  
 Asp Leu Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile  
 35 40 45  
 gca ctt gcc act gtg ctg ttt ttg att ggc gcc ttt cta att att ata 312  
 Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile  
 50 55 60  
 ggc tcc ctg ctg tca ggc tac atc agc aaa ggg ggg gca gac cgg 360  
 Gly Ser Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg  
 65 70 75  
 gcc gtt cca gtg ctg atc att gcc att ctg gtg ttc cta ccc gga ttt 408  
 Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe  
 80 85 90  
 tac cac ctg cgc atc gct tac tac gca tcc aaa ggc tac cgt ggt tac 456  
 Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr  
 95 100 105 110  
 tcc tat gat gac att cca gac ttt gat gac tagaaccac ccca 500  
 Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp  
 115 120  
 tagctgagga ggagtcacag tgcactgtc ccaacttta gatctctagc agaaactata 560  
 gctggagact aaggaattct gcagcttga gatgtttaag aaataatgg ccaagtttt 620  
 tgggccttc ccaagatgtc taagtgaac taacgttagc taattagac aagctcatt 680  
 ttccatccct gggcctcga aagttttcc acaggaatat gtaicatgga agaatagagg 740  
 ttctctgtta atgaaatgt gtgcctgcg accacccctc gttagagctga gcaattcttt 800  
 taaatagct taatgcaca ttgttctctg tagaatagg aacataggg tatgctaact 860

64/177

ttctattat taagtagtt attttaana tatctagta taltctctg tacattacc 920  
 cctacctta tgttccagtg gaagacctta gtaaatcaa agataagctga gtcaattgt 980  
 aatatlttt ttacttgct tcttactgac agcaaccagg aatttttta tctctgagag 1040  
 caagtttca aaatgnaat acttccctg tttaacagtc ctggagccat tctgatacag 1100  
 ttcaacagta gtttggacag cataatait gcaatcatt gtcccttga aatcaagatg 1160  
 ttctgcagat taltcctta accgcggagc ttttgtctgt ttccctaaga aacatgtagt 1220  
 ggtattat taagtttat agcgtatg cttagacct gttagatgac atcaattctg 1280  
 taatgattcc aagatcacgc ctgatgct agaggaatag atcaacttag ttgatctca 1340  
 ttattagct tgaanaagt gacttatatt ccaaggaat taatatgtg aatccaat 1400  
 cctagaata aatgagta acttc 1425  
 10  
 <210> 61  
 <211> 307  
 <212> PRT  
 <213> Homo sapiens  
 15  
 <400> 61  
 Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp Gly Leu  
 1 5 10 15  
 Pro Leu Ser Ala Ser Thr Asp Tyr Gln Gln Ser Thr Gly Met Gln Gln  
 20 25 30  
 Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln Leu Pro  
 35 40 45  
 Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser  
 50 55 60  
 Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Gln Asn Tyr Pro Asn  
 65 70 75 80  
 Val Leu Ala Phe Ser Phe Leu Asp Gln Leu Gln Lys Gln Phe Ile Thr  
 85 90 95  
 Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe  
 100 105 110  
 Ile Gln Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr Asn Asn  
 115 120 125  
 Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln Thr Gln  
 130 135 140

65/177

Ile Lys Leu Arg Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser  
 145 150 155 160  
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly  
 165 170 175  
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly  
 180 185 190  
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile  
 195 200 205  
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp  
 210 215 220  
 10 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr  
 225 230 235 240  
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser  
 245 250 255  
 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu  
 260 265 270  
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe  
 275 280 285  
 Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala Pro Asp  
 290 295 300  
 Tyr Asp Val  
 305

&lt;210&gt; 62

&lt;211&gt; 183

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 62

30 Met Thr Ala Gln Gly Gly Leu Val Ala Asn Arg Gly Arg Arg Phe Lys  
 1 5 10 15  
 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser  
 20 25 30  
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu  
 35 40 45

35

66/177

Asp Lys Gln Val Pro Asp Thr Ser Val Gln Glu Thr Asp Arg Ile Leu  
 50 55 60  
 Val Glu Lys Arg Cys Trp Asp Ile Ala Leu Gly Pro Leu Lys Gln Ile  
 65 70 75 80  
 5 Pro Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile  
 85 90 95  
 Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala  
 100 105 110  
 Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln  
 115 120 125  
 10 Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu  
 130 135 140  
 Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His  
 145 150 155 160  
 15 Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Phe  
 165 170 175  
 Ser Gly Gly Gly Leu Leu Leu  
 180  
 20 <210> 63  
 <211> 327  
 <212> PRT  
 <213> Homo sapiens  
 25 <400> 63  
 Met Arg Ala Leu Pro Gly Leu Leu Glu Ala Arg Ala Arg Thr Pro Arg  
 1 5 10 15  
 Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Arg Pro Ser Ser Ala  
 20 25 30  
 30 Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro Pro Leu Arg Glu  
 35 40 45  
 Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His Asn Ile Ser Leu  
 50 55 60  
 Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile Thr Leu Glu Arg  
 65 70 75 80

35

67/177

Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu  
85 90 95  
Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Gln Gln Leu Gln Asn  
100 105 110  
5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg  
115 120 125  
Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe  
130 135 140  
Arg Gln Gln Lys Gln Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Gln  
145 150 155 160  
10 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr  
165 170 175  
Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp  
180 185 190  
15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn  
195 200 205  
Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Gln Thr Lys Leu Lys Ile  
210 215 220  
Thr Gln Leu Leu Gln Asp Gly Gln Ser Tyr Trp Cys Arg Ala Leu  
225 230 235 240  
20 Phe Gln Leu Gly Gln Ser Gln Gln His Ile Gln Leu Val Val Leu Ser  
245 250 255  
Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Gln Val Ile  
260 265 270  
25 Leu Leu Val Ala Thr Ile Leu Leu Cys Gln Lys Tyr Thr Gln Lys Lys  
275 280 285  
Lys Lys His Ser Asp Gln Gly Lys Gln Phe Gln Gln Ile Gln Gln Leu  
290 295 300  
Lys Ser Asp Asp Ser Asn Gly Ile Gln Asn Asn Val Pro Arg His Arg  
305 310 315 320  
30 Lys Asn Gln Ser Leu Gly Gln  
325

&lt;210&gt; 64

&lt;211&gt; 223

68/177

<212> PRT  
<213> Homo sapiens  
<400> 64  
6 Met Lys Phe Val Pro Cys Leu Leu Leu Val Thr Leu Ser Cys Leu Gly  
1 5 10 15  
Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Gln Gln  
20 25 30  
Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro Ser  
35 40 45  
10 Ser Leu Gly Gln Gly Ala Gly Gln Val Trp Leu Arg Val Asp Cys Arg  
50 55 60  
Asn Thr Asp Gln Thr Tyr Trp Cys Gln Tyr Arg Gly Gln Pro Ser Met  
65 70 75 80  
15 Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu  
85 90 95  
Gln Gln Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu  
100 105 110  
Arg Pro Ser Val Cys Arg Gln Ala Gly Pro Gln Ala His Met Gln Gln  
115 120 125  
20 Val Thr Ser Ser Leu Lys Gly Ser Pro Gln Pro Asn Gln Gln Pro Gln  
130 135 140  
Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Gln  
145 150 155 160  
25 Ala Thr Gln Leu Leu Gly Lys Asp Ser Met Gln Gln Leu Gly Lys Ala Lys  
165 170 175  
Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro  
180 185 190  
Gly Gly Asn Gln Gln Ala Lys Lys Lys Ala Trp Gln His Cys Trp Lys  
195 200 205  
30 Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly  
210 215 220

&lt;210&gt; 65

&lt;211&gt; 48

69/177

70/177

<212> PRT  
<213> Homo sapiens

&lt;400&gt; 65

5 Met Arg Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg

1 5 10 15

Ser Glu Ala Ser Ala Asn Leu Gly Val Pro Ser Lys Arg Leu Lys

20

25

Met Gln Tyr Ala Thr Gly Pro Leu Lys Phe Gln Ile Cys Val Ser

35

40

45

&lt;210&gt; 66

&lt;211&gt; 371

&lt;212&gt; PRT

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 66

Met Ala Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val

1

5

10

15

20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met

20

25

30

Ala Glu Gly Cys Gly Ser Lys Glu His Ser Phe Gln His Pro Phe

35

40

45

Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala

50

55

60

Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Val

65

70

75

80

Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu

85

90

95

30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr

100

105

110

Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr

115

120

125

Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln

130

135

140

Trp Leu Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu

145

150

155

160

Ala Asp Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val

165

170

175

5 Ile Thr Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile

180

185

190

Gln Met Val Leu Glu Lys Phe Val Tyr Lys His Asn Val His Pro

195

200

205

Leu Arg Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser

210

215

220

Leu Leu Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly

225

230

235

240

Asn Pro Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val

245

250

255

15 Gly Gln Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser

260

265

270

Ile Ala Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser

275

280

285

Ala Thr Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp

290

295

300

Ala Leu Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile

305

310

315

320

Leu Gly Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu

325

330

335

25 His Arg Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu

340

345

350

Glu Ser Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn

355

360

365

Asp Ala Ser

370

&lt;210&gt; 67

&lt;211&gt; 90

&lt;212&gt; PRT

35 &lt;213&gt; Homo sapiens



71/177

<400> 67  
Met Phe His Gln Ile Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile  
1 5 10 15  
5 Leu Asn Ser Ile Tyr Gln Cys Pro Gln His Ser Gln Leu Thr Thr Leu  
20 25 30  
Gly Val Asp Gly Lys Gln Phe Pro Gln Val His Leu Gly Gln Trp Tyr  
35 40 45  
Phe Ile Ala Gly Ala Ala Pro Thr Lys Gln Gln Leu Ala Thr Phe Asp  
50 55 60  
10 Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met  
65 70 75 80  
Gln Leu His Leu Arg Ala Thr Ile Arg Met  
85 90  
15  
<210> 68  
<211> 499  
<212> PRT  
<213> Homo sapiens  
20  
<400> 68  
Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu  
1 5 10 15  
Ala Ile Gly Ala Ala Ile Phe Gln Val Leu Gln Gln Pro His Trp Lys  
20 25 30  
Gln Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Gln  
35 40 45  
Phe Pro Cys Leu Gly Gln Gln Gly Leu Asp Lys Ile Leu Gln Val Val  
50 55 60  
30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe  
65 70 75 80  
Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile  
85 90 95  
Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg  
100 105 110

72/177

Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr  
115 120 125  
Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu  
130 135 140  
6 Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile  
145 150 155 160  
Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val  
165 170 175  
10 Ile Pro Pro Phe Val Phe Met Val Thr Gln Gly Trp Asn Tyr Ile Gln  
180 185 190  
Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp  
195 200 205  
Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg  
210 215 220  
15 Tyr Phe Val Gln Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu  
225 230 235 240  
Phe Val Asn Trp Lys Val Ser Met Phe Val Gln Val His Lys Ala Ile  
245 250 255  
Lys Lys Arg Arg Arg Arg Lys Gln Ser Phe Gln Ser Ser Pro His  
260 265 270  
20 Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val  
275 280 285  
Asn Ile Phe Ser Phe Leu Ser Lys Lys Gln Gln Thr Tyr Asn Asp Leu  
290 295 300  
25 Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gln  
305 310 315 320  
Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Leu Pro Ala  
325 330 335  
Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val  
340 345 350  
30 Pro Thr Leu Gln Gln Val Ser Gln Thr Leu Arg Ser Lys Gly His Val  
355 360 365  
Ser Arg Ser Pro Asp Gln Gln Ala Val Ala Arg Ala Pro Gln Asp Ser  
370 375 380  
35 Ser Pro Ala Pro Gln Val Phe Met Asn Gln Leu Asp Arg Ile Ser Gln

73/177

74/177

385 390 395 400  
Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln  
405 410 415  
Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu  
420 425 430  
Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Ser  
435 440 445  
Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe  
450 455 460  
10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser  
465 470 475 480  
Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro  
485 490 495  
Lys Gly Thr  
15  
<210> 69  
<211> 106  
<212> PRT  
20 <213> Homo sapiens  
<400> 69  
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1 5 10 15  
25 Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr Arg Glu Lys Leu Thr Pro  
20 25 30  
Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys  
35 40 45  
Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile  
50 55 60  
30 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser  
65 70 75 80  
Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Arg  
85 90 95  
35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

100 105  
<210> 70  
<211> 152  
5 <212> PRT  
<213> Homo sapiens  
<400> 70  
Met Asp Tyr Val Cys Cys Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp  
1 5 10 15  
Glu Thr His Phe Thr Val Ile Ile Thr Ser Val Gly Leu Glu Lys Leu  
20 25 30  
Ala Gln Lys Gly Lys Ser Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile  
35 40 45  
15 Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys  
50 55 60  
Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu  
65 70 75 80  
Thr Glu Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Glu Asp Ala Leu  
85 90 95  
20 Asp Asp Phe Gly Ile Tyr Glu Phe Val Ala Phe Pro Asp Val Ser Gly  
100 105 110  
Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser  
115 120 125  
25 Gly Gln Asp Leu His Ser Thr Val Tyr Glu Val Ile Gln His Ile Pro  
130 135 140  
Ala Gln Gln Gln Asp His Pro Glu  
145 150  
30 <210> 71  
<211> 921  
<212> DNA  
<213> Homo sapiens  
35 <400> 71

75/177

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tctactgatt atgatacaag caacaggaatg caagatgtca gaaagtatt taantgctt 120  
tcgagagaaac ttgctcaact tccctataga tgtacactga aaacttgaca ttataacatt 180  
aatcttatca gctctctggg agtgaactac atgagtgtgt gcaactgaaa ttaccaaat 240  
gtctcgcct tcccttcct gtagtgctt cagaaggagt tcaatctac ttataacatg 300  
atgaaagcaaa atactcgtgt cagacacatc tgtttcattg aatttgataa cttaattcag 360  
aagacacaagc agcagatataa taatcccaag tccctttcaa caaagataaa tctttctgac 420  
atgcaagacgg aaatcaagct gaggcctcct tatcaaatl coactgtgca actgggggtca 480  
gcaaatggag tcaatcagc atttctcgtt gactgttaag gtgtgtgaa gatttctct 540  
gtcaacacagc gactggaaoc agaacctctg tcaaggatlg taagattat ccttagctt 600  
ttatgtgag cctcgaaatt aattcgagc tttaatgtca taagaagct cctgagagat 660  
gtctgtgtatg attttatata cactattgca ttttcctlg gaacagcagc ctgctttac 720  
caggttatt taactgtca ctacacagc tggcgaaatg tcaaatctt ttgacttlt 780  
ggcttaact gtctatgcaa catgtatcc tatgaactgc gcaacctctg gaacttttc 840  
ttctaatgta ctgtggagc atttgttcaa ctacagatct ggttaaggca agcccaaggc 900  
aagctcccg attatgagt c 921

&lt;210&gt; 72

&lt;211&gt; 549

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 72

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ctaagccggc ctggagagag cagcaggggt cgaagtgaac ggggaggtgg coaggagagac 120  
tcgcctaac cagtcggtta ctggagcaag caagtgcctg atacaaggtt gcaagagaaa 180  
gaacggatcc tggtagagaa ggcgtgtgg gacatgcct tggctccct caaacagatt 240  
cccatgatat tcttcatcat gtacatgga ggcataacta tctcatctt cactaatag 300  
atggtgtgta tgaatgcctt gcaaccacat caggacacta tggccatttc agcaatttc 360  
aagatgttaa aaagtcaag ccaagaattt cttaagggtt tggttatcc catlygaaac 420  
ctgagtgttt tggactggc tgtttacaag tgcaggtcaa tgggaatgtt acctaacat 480  
gcatcgattt gtttagcctt catlgagcc cctgagagaa tggagttaag tggtagagaa 540  
ctgctttg 549

&lt;210&gt; 73

76/177

<211> 981  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 73

atgagggccc tcccgggctt gctggagggc agggcgctta cggccgggct gctctctc 60  
cagtgctctc tgcctgcgcg ggcgccaaag tggcgagag gcaatggccc agattgcct 120  
tttaacagtc caactctcag agaaagata atggcaata accttccct ggaagatcat 180  
aaatctaac tgaactgaaa ttctagtat coagtagaaa aaatatcac tttagaagg 240  
ccttcaatg taattctaac atgcagttc aaacatctg gggatttga tgaagttaat 300  
gtgacttga aaagaatlg tgaacactt ggaatattt atcttgtcag tgaacagga 360  
agaaacttgt ataccacata cagttcac atcatitaa gcaacaaat gggaaatcat 420  
tcttgttct ttcgagagaa aaggaacaa aggggaactt ttatttcaa agtccctgaa 480  
cttcaatgga aaacaaagcc atgtatctt taagttagtg atctcactgt ctgacatgt 540  
aaatgtcaaa attgtttcc tttaattgg acctgtgaa gtatcaatlg gactgttaag 600  
gtccctgttg gtttcaaat gaataaatat gttatcatg gaacatatgc taaggaaaa 660  
aagctgaaga taacaacat tttagagaa gatggggaat cttaactgtg ccgtgcacata 720  
ttcaattag gcgagatga agaacacat gactgttgg tgcctagata ttgttgccc 780  
ctaaacacat ttcttgaat agtgcctag gtgattctt taagtgcac catctcctt 840  
tgtgaagaat acacacaaa gaaagaagag caatcagatg aggggaagaa atttgagag 900  
attgaacagc tgaatcaga tgaatgaat ggtatagaaa ataatgtccc caggtataga 960  
aaatgaagt ctcgtggca g 981

&lt;210&gt; 74

&lt;211&gt; 669

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 74

atgaagtccg tcccctgct cctgtgtgt accttgcct gcttggggac ttgtgtcag 60  
ggcccgaggg aaaaagcaag aagacatgg gaggaaatcc atttccagac tggagggaaa 120  
gattcctgca ctatgtccc cagcagcttg gggcagatg ctgagaaat ctgcttcg 180  
gtcgaactgc gcaaanagaa ccaagactac tgggtgtgagt acaaggggga gscacagatg 240  
tgcagagctt tgcctgtga cccaatct taactgatac aagccctgca ggaactgag 300  
cgctctcac atgctgtgca gggggcccg gttgttagc catcctgtg caggagagct 360

77/177

6 ggacccagg ccacatgca gcaagtgact tcaagctca agggagccc agagcccac 420  
cagcagctg aggtctgggac gccatctcty agggccaaagg ccaagtgaa actacagaa 480  
gcacacagc tgggaagga ctgatggaa gactgggaa aagccaaacc caccaccga 540  
cccacagcca aactaccca gcttgagcc aggcgggag ggaatgagga agcaagaag 600  
aaggctggg aacattgtg gaacccttc caggccctgt ggcctttat ctaagcttc 660  
ttccgaggg 669

&lt;210&gt; 75

&lt;211&gt; 144

10 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 75

15 atgagcttc tgcgtctct cctagtggc gctctgca tggccggag caggcctcg 60  
gcaatctgg gggcgctgc cagcaagaga ttaagatgc agtacgcc aggcgcgtg 120  
ctcaagttcc agatttgtt ttc 144

&lt;210&gt; 76

&lt;211&gt; 1113

20 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

25 atggctgga ccaagtacca gctgttctcty gccggggtca tgttgttac cggctccatc 60  
aacacgtct cggcaaatg ggcggacaat ttcatggccg agggctgttg agggagcaag 120  
gagcacagct tcaagatcc ctctccacag gcagtgggca tgttcttgag agaatctcc 180  
tgtctgctg cctctacct cctccatgc agagtgcaag ggaatcaga ctccagctta 240  
gaccccaagc agcccttcaa cctcttctt ttctggccc cag-gctcty tgacatgca 300  
gggacagcc tcatgtatgt ggtcttgaa atgaccagtg cctccagctt ccagatgcty 360  
cgggtgtag tcatcattt cacttgcttg ttctggttg ccttctggg ccggagcty 420  
gtctgagcc agtggctggg catctagcc accatcgcc ggcgtgtgt cgtgggcty 480  
gttgacctc tgaagcaga cgacagtcc cacaagctca gcgaagtgt cacagggag 540  
ctgtgatca ttatggcca gatcattgt gccatccaga tgggtgtaga ggagaagtc 600  
gttacaac acaatgca ccaactggg gcagttggc ctgagggct ctttggctt 660  
gtatctct cctgtgtgt ggtgccatg tactacatc ccgcggctc ctccagcga 720

78/177

5 aacctctg ggacactgga ggaatgctg gacgctctt gccaggtgg ccagcagccg 780  
ctcatctcg tggactgct gggcaacatc agcagcttg cctttctaa cttecgagge 840  
atcagctca ccaaggaact gacgcaccc accgcctgg tgttgacag cttegcacc 900  
gttgcctct tggcactgag cctggcactg ggtggggagg ccttcactg actgcagatc 960  
cttgcttcc tcaactctc tataggact gcccttaca atgggtaca ccgtccctg 1020  
ctggggcgcc tgcacagggg ccggccctg gcagaggaga gcgagcagga gagaactgtg 1080  
ggtggcacc gactcccat caatgatgc agc 1113

&lt;210&gt; 77

10 &lt;211&gt; 270

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

15 atgttccac aaattgggc agctctgct tactctatg gtattactc taactccatc 60  
taccagccc ctggcaccg tcaactgca actctggcg tggatggaa ggaattccca 120  
gagttcaact tgggcaagt gtaatttato gcaggggag ctcccacaa ggagaggtg 180  
gcaactttg acctatgga caacattgtc ttaatatgg ctgttggtc tgcccagatg 240  
cagttccac ttgtgctac catccgcatg 270

&lt;210&gt; 78

&lt;211&gt; 1497

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 78

25 atggtggacc ggggcctct gctacactcg gccatcatc ttacctggc catcgggggc 60  
ggatcttcy aagtgtgga ggaaccaccc tggagggagg ccaagaaaa ctactacaa 120  
cagaagctg actctgtaa ggaattcccg tgcctgggic agggggcct ggacaagatc 180  
ctagaggtgg tatctatgc tgaaggacag ggtgtggcca tcaagggaa ccagacctc 240  
aacactgga actggcccaa tgaatgatt tttagcaga cgtcttacc caccattgga 300  
tatggcaatg tggctccaa gaccccgcc ggtgcctct tctgtgttt ctatggtctc 360  
ttgggggtgc cctctgctc gacgtggtc agtgcctgg gcaagtctt cgggggagct 420  
gcaagagac tagggaatt ccttaccag agaggtgtga gtctcgga ggcgcagatc 480  
acgtgcacag taactctat cgtgtgggg gtcctagtc acctgtgat cccaccttc 540

79/177

gtatcatg tgactaggg gtgaaactac atcgagggcc tctactact cttatcacc 600  
 atctccacca tccgtctcgg tgactttgtg gccgtgtgaa accccagcgc caactcaaac 660  
 gccctgtacc gctactcgt ggaagctotgg actacttgg ggttggcctg gcttccact 720  
 ttgtccaaat ggaaggttgg catgtttgtg gaagtccaaa aagcattaa gaacggggcg 780  
 cggcgaaagg aagagctctt tgaagctacc ccaactccc ggaagggcct gacgttgaag 840  
 gggagcaagg cctccaaagg cgtcaacatc tcaagctta ttcccaaaa ggaagagacc 900  
 tacaacgacc tcatcaaggaa gacggggaaag aagccatga agcaagcgg ggttgggggg 960  
 aaggcccccgg gcccaagggtt gggggctcaa ggggttggc tcccaggaat gccctctcc 1020  
 ctggttccccc tggatgctta ctccaaagac cgggttggca ccttggaaag ggtgtccacg 1080  
 acactgagga gcaaaaggcca cgtatcaagg tcccagatg aggaaggtctt ggcacggggc 1140  
 cctgaagaca gctccctcgc ccccgagggtt ttcattgaac agcttggacc catcaaggag 1200  
 gaatcgagag catgggacgc ccaagactac caacactaa tcttcaagg cgcacagacc 1260  
 accttcctga acacggagggc tggccttcaa gacgaaggaa cctccaaagt ctgcctagag 1320  
 gcaacttgg caaggagagg gagccccag cagggggttg aagcaaggc gccctgaac 1380  
 atgggcagat tccctctcc ctccaggtcc accttcaaaa gaactgaagc tgaactctc 1440  
 gtgcctacg aacagctgat gaatgaatga acaagagcta aacgcccaca gggacaa 1497

<210> 79  
 <211> 318  
 <212> DNA  
 <213> Homo sapiens

<400> 79  
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 cagcgtatcg acccgactcg ggaagagtg aaacccagag aactgaatic catcgagcag 120  
 gggagcttg cccaagtga gaagtctca ccaaggggcg gaaccggaa catcgtgaac 180  
 ggcctaggaa tccggccct ggtgttggct atttatggt aaactctta ctgcatttcc 240  
 caggagcgtt tccatagta gctagaagc gaagcaaaag ctgcaggag ccgagctctg 300  
 gcaaggcgt cagggtcc 318

<210> 80  
 <211> 456  
 <212> DNA  
 <213> Homo sapiens

80/177

<400> 80  
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 aacgtatca tcaactcgt aggaactggag aagcttgcac agaagagaaa atcattgtca 120  
 ccttgaaga gtaaacctg aatcacctta tttttgatta tatccattgt tcttctcttc 180  
 ctatgaaaa aatatcaacc ctacaaggtt ataaacaga aactagaag caggccagaa 240  
 aacagatcaa ggaagcttca aacttttca ggcacatgaag atgccttga tgacttcgga 300  
 atatatgaat ttgttgcctt tccagatgtt tctgtgttt ccagatccc aagcaggtct 360  
 gtccagcct ctgatttgtt atcggggcaa gatttgaaa gtacagctga tgaagtatt 420  
 cagcacctcc ctgcaccagca gaagaccat ccaagag 456

<210> 81  
 <211> 1436  
 <212> DNA  
 <213> Homo sapiens  
 <220>  
 <221> CDS  
 <222> (66)...(989)

<400> 81  
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 ttgaa atg tct atg att tta tct gcc tca gtc att cgt gtc aga gat 107  
 Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp

1 5 10  
 gga ctg cca ctt tct gct tct act gat tat gaa caa agc aca gga atg 155  
 Gly Leu Pro Leu Ser Ala Ser Thr Asp Tyr Glu Gln Ser Thr Gly Met  
 15 20 25 30  
 cag gag tgc aga aag tat ttt aaa atg ctt tcc agg aaa ctt gct caa 203  
 Gln Glu Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln  
 35 40 45  
 ctt cct gat aga tgc aca ctg aaa act gga cat tat aac att aat ttt 251  
 Leu Pro Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe  
 50 55 60  
 att agc tct ctg gga gtc agc tac atg atg ttg tgc act gaa aat tac 299  
 Ile Ser Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr  
 65 70 75

82/177

255 260 265 270 285  
 tat gaa ctg cgc aac ctc tgg cag ctt ttc ttt cct gtc act gtc gga  
 Tyr Glu Leu Arg Asn Leu Trp Gln Phe Phe His Val Thr Val Gly  
 5 gca ttt gtt aca cta cag atc tgg cta agg cca gcc cag ggc aag gct  
 Ala Phe Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala  
 290 295 300  
 ccc gat tat gat gtc tgaaccatc cttaagatct attgcttgg ettc  
 Pro Asp Tyr Asp Val  
 305  
 10 agggggataa ggagggaaca tatcataact gaactgtgat gaagaagctg tccccacag  
 aggaagact ctgctttctt tctctcaac tttcttttt taaaatcagc atgctgtgac  
 tctgagcatg gaagagctct ctcaagaaga tctggccat gagaactatca ttcagaggag  
 gaggggattt ctctcttcaa ggcataaaca gtggagaac agtcatatgc catgggaagt  
 15 ctggccagc agtctgaaat ccttctcgaa gagtgcaga aatagatgtg gtattgtctt  
 gaggaaccag caggaggaaac tctcaacct gagtgtgect tctgaggca ttagtataga  
 ccaataaaa agctgcagaa attggaaagt ttatgtttta aataaatgac tctgat  
 1436

<210> 82  
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 <212> DNA  
 <213> Homo sapiens  
 <220>  
 <221> CDS  
 <222> (87)...(638)

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 cgaggctata ggacgagct gttgcc atg acg gcc cag ggc ctc gtc gtc  
 Met Thr Ala Gln Gly Leu Val  
 30 1  
 5  
 gct aac cga ggc cgc ttc aag tgg gcc att gag cta agc ggg cct  
 Ala Asn Arg Gly Arg Arg Phe Lys Trp Ala Ile Glu Leu Ser Gly Pro  
 10 15 20  
 35 gga gga ggc agc agc ggt cga agt gac cgg ggc agt ggc cag gga gac  
 206

81/177

347  
 cca aat gtt ctc gcc ttc ttc ttc ctg gat gag ctt cag aag gag ttc  
 Pro Asn Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe  
 80 85 90  
 att act act tat aac atg atg aag aca aat act gtc aga cca tac  
 Ile Thr Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr  
 95 100 105 110  
 tgc ttc att gaa ttt gat aac ttc att cag agg acc aag cag cga tat  
 Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr  
 115 120 125  
 10 aat aat ccc agg tct ctt tca aca aag ata aat ctt tct gac atg cag  
 Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln  
 130 135 140  
 acg gaa atc aag ctg agg cct cct tat cca att tcc atg tgc gaa ctg  
 Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu  
 145 150 155  
 ggg tca gcc aat gga gtc aca tca gca ttt tct gtt gac tgc aac ggt  
 Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly  
 160 165 170  
 20 gct ggt aag att tct tct gct cac cag cga ctg gaa cca gca act ctg  
 Ala Gly Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu  
 175 180 185 190  
 tca ggg att gta gga ttt atc ctt agt ctt tta tgc gga gct ctg aat  
 Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn  
 195 200 205  
 25 tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt  
 Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly  
 210 215 220  
 gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc  
 Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys  
 225 230 235  
 30 ctt tac cag tgc tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc  
 Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val  
 240 245 250  
 aaa tct ttt ttg act ttt ggc tta atc tgc tta tgc aac atg tat ctc  
 Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu  
 255 260 265 270 275 280 285 290 295 300 305 310 315 320 325 330 335 340 345 350 355 360 365 370 375 380 385 390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620 625 630 635 640 645 650 655 660 665 670 675 680 685 690 695 700 705 710 715 720 725 730 735 740 745 750 755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995

83/177

Gly Gly Ser Arg Gly Arg Ser Asp Arg Gly Ser Gly Gln Gly Asp  
25 30 35 40  
tcg ctc tac cca gtc ggt tac ttg gac aag caa gtc cct gat acc agc 254  
Ser Leu Tyr Pro Val Gly Tyr Leu Asp Lys Gln Val Pro Asp Thr Ser  
5 45 50 55  
gtg caa gag aca gac cgg atc ctg gtc gag aag cgc tgc ttg gac atc 302  
Val Gln Gln Thr Asp Arg Ile Leu Val Gln Lys Arg Cys Trp Asp Ile  
60 65 70  
gac ttg ggt ccc ctc aaa cag att ccc atg aat ctc ttc atc atg tac 350  
Ala Leu Gly Pro Leu Lys Gln Ile Pro Met Asn Leu Phe Ile Met Tyr  
75 80 85  
atg gca gac aat act atc tcc atc ttc cct act atg atg gtc tgt atg 398  
Met Ala Gly Asn Thr Ile Ser Ile Phe Pro Thr Met Met Val Cys Met  
90 95 100  
atg gcc tgg cga ccc att cag gca ctt atg gcc att tca gcc act ttc 446  
Met Ala Trp Arg Pro Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe  
105 110 115 120  
aag atg tta gaa agt tca agc cag aag ttt ctt cag ggt ttg gtc tac 494  
Lys Met Leu Gln Ser Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr  
125 130 135  
ccc att ggg aac ctg atg ggt ttg gca ttg gct gtt tac aag tgc cag 542  
Leu Ile Gly Asn Leu Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln  
140 145 150  
tcc atg gga ctg tta cct aca cat gca tcc gat tgg tta gcc tto att 590  
Ser Met Gly Leu Leu Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile  
155 160 165  
gag ccc cct gag aga atg gag ttc agt ggt gga gga ctg ctt ttg tgaac 640  
Glu Pro Pro Glu Arg Met Glu Phe Ser Gly Gly Leu Leu Leu  
170 175 180  
atgagaagc agcgctggt acctatgat ttgggtcta ttacatcct tcttaagcc 700  
cagtgctcc tcaagatct cttaactaa tcaatttgt taagaagac caaagctcc 760  
ttttccat ggtgggtga caggtccctg aaggaatgt tgcatttac gaaacaca 820  
aagaactat acctaaccc aaggtgaa ataatgtaga aaacttatt ttgtttcca 880  
gtcagagca aaaaacaa aaaaaaat aaatgttaa acaaggaat aactgtgct 940  
aaataagaa ctgtgagc atctcttc aataataa atgttgaga acaatgc 997

84/177

<210> 83  
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<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS  
<222> (134)...(1117)  
6  
10 <400> 83  
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gggaacttgg acaacggag cggagagctg agggagagat cctcaagagg acccaagcgg 120  
acctctggc gcc atg cgc gcc ctc ccc ggc ctg gtc gag gcc agt ggc 169  
Met Arg Ala Leu Leu Pro Gly Leu Leu Gln Ala Arg Ala  
15 1 5 10  
cgt acg ccc cgg ctg ctc ctc cag tgc ctt ctc gcc gcc ggc cgc 217  
Arg Thr Pro Arg Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Arg  
15 20 25  
cca agc tgg gcg gac ggc agt gcc cca gat tgg cct ttt aca agt cca 265  
Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro  
30 35 40  
cct ctc aga gaa gaa ata atg gca aat aac ttt tcc ttg gag agt cat 313  
Pro Leu Arg Gln Gln Ile Met Ala Asn Asn Phe Ser Leu Gln Ser His  
45 50 55 60  
aac ata tca ctg act gaa cat tct agt atg cca gta gaa aaa aat atc 361  
Asn Ile Ser Leu Thr Gln His Ser Ser Met Pro Val Gln Lys Asn Ile  
65 70 75  
act tta gaa agc cct tct aat gta aat ctc aca tgc cag ttc aca aca 409  
Thr Leu Gln Arg Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr  
80 85 90  
tct ggg gat ttg aat gca gta aat gtc act tgg aaa aaa gat ggt gaa 457  
Ser Gly Asp Leu Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Gln  
95 100 105  
caa ctt gag aat aat tat ctt gtc agt gca aca gga agc acc ttg tat 505  
Gln Leu Gln Asn Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr

85/177

110 115 120  
acc caa tac agg ttc acc att aat agc aaa caa atg gga agt tat 553  
Thr Gln Tyr Arg Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr  
125 130 135 140  
tct tgt ttc ttt cga gag gaa aag gaa caa agg gga aca ttt aat ttc 601  
Ser Cys Phe Phe Arg Glu Glu Lys Glu Arg Gly Thr Phe Asn Phe  
145 150 155  
aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta 649  
Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val  
160 165 170  
ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta 697  
Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu  
175 180 185  
aat tgg acc tgg tac agt agt aat ggg agt gta aag gtt cct gtt ggt 745  
Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly  
190 195 200  
gtt caa atg aat aaa tat gtg atc aat gga aca tet gct aac gaa ace 793  
Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr  
205 210 215 220  
aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg 841  
Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp  
225 230 235  
tgc cgt gca cta ttc caa tta ggc gag agt gaa gaa cac att gag ctt 889  
Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu  
240 245 250  
gtg gtg ctg agc tat ttg gtg ccc ctc aaa cca ttt ctt gta ata gtg 937  
Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val  
255 260 265  
ggt gag gtg att ctt tta gtg gcc acc att ctg ctt tgt gaa aag tac 985  
Ala Glu Val Ile Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr  
270 275 280  
aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag 1033  
Thr Gln Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln  
285 290 295 300  
att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc 1081

86/177

110 115 120  
ile glu gln leu lys ser asp asp ser asn gly ile glu asn asn val 1130  
305 310 315  
ccc agg cat aga aaa aat gag tct ctg ggc cag tgaatacaaa acatca  
Pro Arg His Arg Lys Asn Glu Ser Leu Gly Gln  
320 325  
tgtacgaat cattggaga tacaagagt tegtatttca gtttattta tecttctgt 1190  
taagagctc tgagttttta gttttaaaag gatgaaagc ttatgaaaca tgcacagcag 1250  
gagcttacc aacgatatat gtacgatcta aaggtatatt ttoatttgt aattatgta 1310  
cataaagca atgtaaatca gaataaatat gttagaccag aataaatta attatattct 1370  
ggtcttcaa ggacacacag aacagatatac agcagaatca cttaatactt catagaacaa 1430  
aaatcacata aaactgttt ataaccaaag aattcatgaa aagaaagcc ttgcacattt 1490  
gtcttagaaa gttatttttt taanaaaat catacttact attagtatct atggaagtat 1550  
agtaaacat ttattatgtaa aggtcatctt tctgtgatag tgaanaata tgtcttact 1610  
aagttgaat gaatacttcc tgccttttgt catgatagtt attcacaaat ctccaaaga 1670  
aaataatcc ttttaccgg aaatatgggt tttagggcaa taataaaac tgtcttgtct 1730  
ctaaagtct gcactacaaa agc 1753

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<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS  
<222> (62)...(733)

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c atg aag ttc gtc ccc tgc ctc ctg ctg gtg acc ttg tcc tgc ctg 106  
Met Lys Phe Val Pro Cys Leu Leu Val Thr Leu Ser Cys Leu  
1 5 10 15  
ggg act ttg ggt cag gcc ccg agg caa aag caa gga agc act ggg gag 154  
Gly Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Glu  
20 25 30  
gaa ttc cat ttc cag act gga ggg aga gat tcc tgc act atg cgt ccc 202  
Glu Phe His Phe Gln Thr Gly Arg Asp Ser Cys Thr Met Arg Pro



5	gaagattca atactgaacg catcatgaa ttccacagct tcaagtaata gcacgtatgt gtctgcaaaa taagaagatg attccag	1090	1117
10	<210> 85 <211> 1380 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (43)...(189)		
15	<400> 85 gcagctctgc tgaaggcggc cgaagtgcct ggcctactta ag atg aag ctt ctg Met Arg Leu Leu	54	
20	ctg ctt ctg cta ctg gtc gcg tct gcg atg gtc cgg agc gag ggc tgg Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Gln Ala Ser	102	
25	5 10 15 20 gac aat ctg ggc ggc gtc ccc agc aag aga tta aag atg cag tac ggc Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala	150	
30	25 30 35 aag ggg ccg ctg ctg aag ttc cag att tgt gtc tcc tggg Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser	190	
35	40 45 gttaagagcg ggtcttgtag gactgacagc ggtgtattag ccaagcgtae ccagaaatcc gcattgaagc agagaattac ctccctcaac caatatatag acaatagaa tcttctcgt cagctctcaa actagatata ataggtctaa taattgttgg caagatccct ttgcttct ttgcacatga agctctcagc atctgcagcgt ggggcacaga aatataggt tatgcagtta tgatgttttt ctctctgagc acaatgatct agaacagctg tatgcacaaa ggtgcatttg agataacttt aaatgatga cctgtgtggt ctaagctgga atctgacac ctccatcaaa tgcacaact tgttcaact cttagacatg aaatgagcct caatgtcat atgattcaaa	250	250

248 gaa gta ggc atg ttc ctg gga gaa ttc tcc tgc ctg gct gcc ttc tac  
Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala Phe Tyr  
55 60 65  
296 ctc ctc cga tgc aga gct gca ggg caa tca gac tcc agc gta gac ccc  
Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val Asp Pro  
70 75 80  
344 cag cag ccc ttc aac cct ctt ctt ttc ctg ccc cca gcg ctc tgc gac  
Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Ala Leu Cys Asp  
85 90 95  
392 atg aca ggg acc agc ctc atg tat gta gct ctg aac atg acc agt gcc  
Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala  
100 105 110  
440 tcc agc ttc cag atg ctg cgg ggt gca gta atc ata ttc act ggc ctg  
Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Phe Thr Gly Leu  
115 120 125 130  
488 ttc tgc gta gcc ttc ctg ggc cgg agc ctg ctg agc cag tgg ctg  
Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln Trp Leu  
135 140 145  
536 ggc atc cta gcc acc atc gta ggg ctg gta gta ggc ctg gct gcc  
Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Gly Leu Ala Asp  
150 155 160  
584 ctc ctg agc aag cag cag agt cag cag cag cag gaa gta atc aca  
Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val Ile Thr  
165 170 175  
632 ggg gac ctg tta atc atc atg gcc cag atc atc gtt gcc atc cag atg  
Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile Gln Met  
180 185 190  
680 gta cta gag gag aag ttc gta tca aca cag aat gta cca cca ctg cgg  
Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg  
195 200 205 210  
728 gaa gtt ggc act gag ggc ctc ttt ggc ttt gta atc ctc tcc ctg ctg  
Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu  
215 220 225  
776 cta gta ccc atg tac tac ccc gcc ggc tcc ttc agc gga aac cct  
Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly Asn Pro  
230 235 240 245 250 255 260 265 270 275 280 285 290 295 300 305 310 315 320 325 330 335 340 345 350 355 360 365 370 375 380 385 390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620 625 630 635 640 645 650 655 660 665 670 675 680 685 690 695 700 705 710 715 720 725 730 735 740 745 750 755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995

670 tccacacca tgcatacatg caccacctat cagcactgaa aactcttttg cattanggga  
730 tcatgcaag agcagcgta ctgacattat gaagcctgt actgaagaca gcaagctgtt  
790 agtaagacc agatgcttct ttggcaggct cgtgtacct ctggaaac ctcaatgcaa  
850 gatagtgtt cagtgctggc atatttggg attctgaca ttcctgagt gcaataaac  
910 tgtatagtt tcccacact ccaaaaac acccagtaa tgggtgtg tggtttttt  
970 tttanggtaa acattactac ttgtaacttt tttctttagt catatttga aaagtagna  
1030 attggttac aatttgatt ttttccaaa gatgtctgtt aaatctgtg tgcittata  
1090 tgaatattg tttttatag tttaaatg atccttggg aatcagttg aagttccaaa  
1150 atactttata agagttttata agacatctct aatttgcca tgcacgttt atcagttta  
1210 caaaatatag cagatgcaag attatgggg aaatctata ttcaggtac tctataatt  
1270 tttgtgatg tgtgtgatg cgtgtgatta cccaggaact actaanaaa ccaactgctt  
1330 tttaaatcct attgtgtagt taagtgtca tgcctgacc aatctaaga attgattaat  
1380 taactgggcc tttatactta actaanaaaa aaactaanga gatagagt

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<212> DNA  
<213> Homo sapiens  
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<221> CDS  
<222> (51)...(1166)  
<400> 86  
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Met Ala  
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tgg acc aag tac cag ctg ttc ctg gcc ggg ctc atg ctt gtt acc ggc  
Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val Thr Gly  
5 10 15  
tcc atc aac acg ctc tgc gca aca tgg ggc gac aat ttc atg gcc gag  
Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met Ala Glu  
20 25 30  
ggc tgt gga ggg agc aag gag cag agc ttc cag cat ccc ttc ctc cag  
Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe Leu Gln  
35 40 45 50

91/177

230 235 240  
cgt ggg aca ctg gag gat gaa ttg ggc ggc ttc tgc cag gtg ggc aag 824  
Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Glu Val Gly Gln  
245 250 255  
cag cag ctc att gcc gtg gca ctg cgc ggc aac atc agc agc att gcc 872  
Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala  
260 265 270  
ttc ttc aac ttc gca ggc atc agc gtc aac aag gaa ctg agc ggc aac 920  
Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser Ala Thr  
275 280 285 290  
acc cgc atg gtg tgc gag agc ttg cgc acc gtc atc tgg gca ctg 968  
Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp Ala Leu  
295 300 305  
agc ctg gca ctg ggc tgg gag ggc ttc cat gca ctg cag atc ctt ggc 1016  
Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile Leu Gly  
310 315 320  
ttc ctc ata ctc ctt ata ggc act gcc ctc tac aat ggg cta cac cgt 1064  
Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg  
325 330 335  
ccg ctg ctg ggc cgc ctg tcc agg ggc cgg ccc ctg gca gag gag agc 1112  
Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser  
340 345 350  
gag cag gag aga ctg ctg ggt ggc acc cgc act ccc atc aat gat gcc 1160  
Gln Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala  
355 360 365 370  
agc tgaagttccc tgaaggtctc taactgcaac cgggtgtctcc ttctccc 1210  
Ser  
tgaagctgag gcaacacagc ctgtgtggcc ccgaatggcc tatcccaag gctcaacct 1270  
gtccacatccc tgcagaabcc ccagggagagc tgcctgcaca gaagataaca acaaccaagt 1330  
ccctctttc taactaacac ctgaagggtg gtgttaccac gcccccacaa gcttggtggc 1390  
agtgacaac cccagctctc tggaccctcc ctacagacct agagctaat catgaagttg 1450  
aatgttagga atttaccac gtaagtatac tgaataataa actagattat cat 1503

35

&lt;210&gt; 87

92/177

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<213> Homo sapiens  
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Met Phe His Gln Ile  
1  
5  
tgg gca gct ctg ctc tac ttc tat ggt att atc ctt aac tcc atc tac 102  
Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile Leu Asn Ser Ile Tyr  
10 15 20  
cag tgc cct gag aac agt caa ctg aca act ctg ggc gtg gat ggg aag 150  
Gln Cys Pro Glu His Ser Gln Leu Thr Leu Gly Val Asp Gly Lys  
25 30 35  
gag ttc cca gag gtc cac ttg ggc cag tgg tac ttc atc gca ggg gca 198  
Glu Phe Pro Glu Val His Leu Leu Gly Gln Trp Tyr Phe Ile Ala Gly Ala  
40 45 50  
gct ccc acc aag gag gag ttg gca act ttt gac cct gtg gac aac att 246  
Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp Pro Val Asp Asn Ile  
55 60 65  
gtc ttc aat atg gct gct ggc tct gcc ccg atg cag ctc cac ctt cgt 294  
Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met Gln Leu His Leu Arg  
70 75 80 85  
gct aac atc cgc atg tgaatgaaa gatgggtctc gtcgtgcccg g 340  
Ala Thr Ile Arg Met  
90  
aatgtgctc accacatgac tgaagggagc acaatctcca gaactgaag ccgacctgac 400  
atgaagacag agctctttc aagtcatgc ccaggtggaa tcatgttcaa tgaagacaggc 460  
cagggttacc agcgctttct cctctacaat cgttaccac atccctccga aaagtgtgtg 520  
gaggaattca agtccctgac ttccgtcctg gactccaag cctcttatt gactccatgg 580  
aatcaagag ccgtgtgagc gtcaatlaac tgacctgtaa cttaactaaa gtccccaagat 640  
gggtacaatg gaagctgagc tgttggaggg agaaagctga gacttccagc tccagctccc 700

35

93/177

94/177

actcaagata ataaagataa ttttcaate ctc	733	Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile	85	90	95
<210> 88		acc acc att gga tat ggc aat gtc ccc aag acc ccc gcc ggt cgc			693
<211> 3768		Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg			
<212> DNA		ctc ttc tgt gtt ttc tat ggt ctc ttc ggg gtc cgc ctc tgc ctg acg	100	105	110
<213> Homo sapiens		Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr			741
<220>		tgg atc agt gcc ctg ggc aag ttc ttc ggg gga cgt gcc aag aga cta	115	120	125
<221> CDS		Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu			789
<222> (358)...(1857)		ggg cag ttc ctt acc aag aga ggt gtc agt ctg cgg aag ggc cag atc	130	135	140
<400> 88		Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile			837
gctagtggcg cgcgagggag cgaacgtgg agaacggcc cactgtcttg cccagagta	60	145	150	155	160
agtcctgtgt tcttcagctt ccttaagcat cgcggttcca gggcgccctt tcagccccc	120				
tgggtttcgc ccaccccggg ccgctgaggt ggggcccac gcaagtcacc gcactccgtg	180				
ggccaaacttg gccaaagcac tctgtccggg gacggtgct tgcggggggt gactaccggg	240				
cactgcgat gcggagctcc aaattcaaac agctgttttc agaggttggg gggcgggcgg	300				
actgtagca gctggggcta ggaagagctt tctctaggag gcggcgctc gggagcc	357				
atg gtg gac cgg ggc cct ctg ctc acc tgg gcc atc ttc ttc tac ctg	405				
Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu		180	185	190	
1	5	10	15		
gcc atc ggg gcg gcg atc ttc gaa gtg ctg gag gag cca cac tgg aag	453				
Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys		195	200	205	
25	20	25	30		
gag gcc aag aaa aac tac tac aca cag aag ctg cat ctg ctc aag gag	501				
Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu		210	215	220	
35	40	45			
ttc ccg tgc ctg ggt cag gag ggc ctg gac aag atc cta gag gtg gta	549				
Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val		225	230	235	
50	55	60			
tct gat gct gca gga cag ggt gtc gcc atc aca ggg aac cag acc ttc	597				
Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe		240	245	250	
65	70	75	255		
aac aac tgg aac tgg ccc aat gca atg att ttt gca gcg acc gtc att	645				
35	260	265	270		

96/177

10	acc gag aag gcc ctg cag atg aag gag aac aac gcc tcc aag gtc	1221
5	Ser Arg Lys Ala Leu Glu Val Lys Gly Ser Thr Ala Ser Lys Asp Val	
275	280	285
5	aac atc ttc agc ttc ctc tcc aag aag gaa gag aac tac aac aac ctc	1269
290	295	300
10	atc aag aag atc gag aag aag gcc atg aag aca agc gag ggt gag gag	1317
305	310	315
10	Ile Lys Glu Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu	
320	325	330
10	acc gag ccg gag cca gag ctg gag cct caa gag ggt gag ctc cca gca	1365
335	340	345
10	Thr Gly Pro Gly Pro Gly Leu Gly Pro Glu Gly Gly Leu Pro Ala	
350	355	360
10	ctg ccc cct tcc ctg gty ccc ctg gta gtc tac tcc aag aac gag gty	1413
365	370	375
10	Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val	
380	385	390
15	ccc acc tgg gaa gag gty tca cag aca ctg aag agc aaa ggc caa gta	1461
395	400	405
10	Pro Thr Leu Glu Glu Val Ser Glu Thr Leu Arg Ser Lys His Val	
410	415	420
15	tca aag tcc cca gat gag gag gct gty gaa ggc gcc gaa gag aac	1509
425	430	435
20	Ser Arg Ser Pro Asp Glu Ala Val Ala Arg Ala Pro Glu Asp Ser	
440	445	450
20	tcc aat gcc ccc gag gty ttc atg aac aag ctg aac cgc atc agc gag	1557
455	460	465
20	Ser Pro Ala Pro Glu Val Phe Met Asn Glu Leu Asp Arg Ile Ser Glu	
470	475	480
25	gaa tgc gag cca tgg gag gcc cag gag tac aac cca ctc atc ttc cag	1605
485	490	495
25	Glu Cys Glu Pro Trp Asp Ala Glu Asp Tyr His Pro Leu Ile Phe Glu	
500	505	510
25	gac gcc agc atc acc ttc gty aac aag gag gct ggc ctc tca gag gag	1653
515	520	525
30	Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu	
530	535	540
30	gag aac tcc aag tcc tcc cta gag gag aac ttc gca gag gag gag agc	1701
545	550	555
35	Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser	
560	565	570
35	ccc cag cag gag gct gaa gcc aag gag ccc ctg aac atg gag gac ttc	1749
575	580	585
35	Pro Glu Glu Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe	

96/177

10	ccc tcc tcc gag tcc acc ttc aac agc act gag tct gag ctc tct	1797
5	Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser	
465	470	475
5	gty cct tac gaa cag ctg atg aat gag tac aac aag gct aac agc ccc	1845
485	490	495
5	Val Pro Tyr Glu Glu Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro	
500	505	510
10	aag gag aca tgaagcagg ccgctccc aaccacact tgaatg	1890
515	520	525
10	Lys Gly Thr	
530	535	540
10	cccttccc cctcaccta ggtgtcccg agatgaccg gacgctggc cctgtgtgg	1950
545	550	555
10	gggacagct cgaactgg agtgggggc caggggact cctaacctc cactacccc	2010
560	565	570
10	agctagatgt atgcacggga caggccctct gtaccacgc tgaacatac cctgtgctg	2070
575	580	585
10	gggacatctg tccatgact ggtgtgtgta tccacacatg caagacatg ctgtgtgctg	2130
590	595	600
10	ggacagtgag gcagacatga cccatggag ccctggact agctgtttta gtttaacgt	2190
605	610	615
10	ttgtgtgagt atcacacgtg tctctgagt ccggggctc agctgtttta gtttaacgt	2250
620	625	630
10	attactgagc tggacatctg gaggaggag tctgaatgt ctggggaggt accgtgtgc	2310
635	640	645
15	gtgggtcag gttttccgt accaagcag gaggagggc cgcgcgac cagctgtg	2370
650	655	660
15	gcctgcaggt caggtgggc acctactaca aacctgagt ggtgtggagc tgcgtggagt	2430
665	670	675
20	gggagtggag agatgagggc aggtgtctca accgtctga ctcacagggc ctggaaaca	2490
680	685	690
20	gtccatgtg ggcctgggc ctgggtcct cactctctt gtgtgttac tcaugccag	2550
695	700	705
20	cccacagtg taaggaggag agtagcagag catgggttac tggagccgg gactgttag	2610
710	715	720
20	gctgtgtgac agggagctgc aagatggag ctacgtatg gctgtgtctg cccctaccc	2670
725	730	735
20	tccgtccgc caggaactg caaacctgc ccgtggcc caggacctgc actccacac	2730
740	745	750
25	ctgtgtctt ctccttccct gtgccttga caagacac actgcgcgc ttcctacc	2790
755	760	765
25	accagccccc ttgggcagag caggtggag ccaaatgtc ctggccacaa aaatgggtga	2850
770	775	780
25	tgtccagata tgtgaactaa gctccttct ctacgtagt ttgaatgac acgtgtggt	2910
785	790	795
30	gcaaatggag tgtgtgcaaa cgaacactg tgaactgtg tgtgtttag aaaggaag	2970
800	805	810
30	atttggtctg gggagcaaa gataatgta aactgtgt ggaactctg gtaggggtg	3030
815	820	825
30	ggaggaact gctgtacta gactctctg gtctccatg atgtccacc tggggctggc	3090
830	835	840
30	caactgtgc ctgaatgtt ttgttatit ttgtttat tttaacaa actgtgtt	3150
845	850	855
35	ttataact ggaactgtc gttgtgtca gaggcagtg ttaagagca ggtgtccaa	3210
860	865	870
35	gattggaga tctagtctt ggcctccgc cctgaacac aattgggct ttlttggtga	3270
875	880	885
35	cctacacaa ggcacatgat tcaaggaca tgtccccag cagagtgga gaaggagca	3330
890	895	900

97/177

ctgaggtgag caaagcagg aaggggcatc caactcggtt gactggaggc cgggcaggaa 3450  
 gcaatgcatc agagcgcgc agctccgttc actctctgcc ttctgcacca ctactctggg 3510  
 gcagtggggc cagagccacc ctcccacaa tftgaagaca gtgatgggca cgtgccacca 3570  
 ccccacttc tctagccgtt tgcagaggcc gccaccacgc aggggacctga aaaggagcag 3630  
 cctcgtattt ttctgaaa tgttttaatg aaccatgtt ttctgtgttg tccctgcatc 3690  
 gcgcacactg tatgtacata ctggcaaga tgcnaaatgt aattatttt aacatttta 3750  
 caataaaca tgaggtgg 3768

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10 <211> 770

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

15 <222> (24)...(344)

<400> 89

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Met Ala Ser Ser Gly Ala Gly Asp Pro Leu

20

gat tet aag cgt gga gag gcc ccg ttc gct cag cgt atc gac ccg act 101

Asp Ser Lys Arg Gly Glu Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr

15

20

25

cgg gag aag ctg aca ccc gag caa ctg cat tcc atg cgg cag gcg gag 149

Arg Glu Lys Leu Thr Pro Glu Gln Leu His Ser Met Arg Gln Ala Glu

30

35

40

ctt gcc cag tgg cag aag gtc cta cca cgg cgg cga acc cgg aac atc 197

Leu Ala Gln Trp Gln Lys Val Leu Pro Arg Arg Thr Arg Asn Ile

45

50

55

gtg acc gcc cta gcc atc ggg gcc ctg gtg ttg gct att tat ggt tac 245

Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr

60

65

70

acc ttc tac tct att tcc cag gag cgt ttc cta gat gag cta gaa gac 293

Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Asp

35 75

80

85

90

98/177

gag gcc aaa gct gcc cga gcc cga gct ctg gaa agg gag tca ggg tcc 361  
 Glu Ala Lys Ala Ala Arg Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser 105  
 95 100  
 taatctgga tgggtattga taatgtccaa cctgctggag ccccttcaca tgggtgatga 400  
 tgcceatga cctgttagaa attgaatcct gctcacaa ttgttgcoct tcttactaac 460  
 ctggaccgtt gattgagccc aagaaaccag ggaactacgc atttggccaa tgcnaaaga 520  
 acagaacttt gcccaactga caactgtctgt gtacaatgac tgaacctttt ctgttagttt 580  
 gttccttgt ttgagagtg tgaatgcgac cgtggotttt ccaaaagttt ctgaacttgt 640  
 ggttacccc ctccaccttc caggagcga gttgttaca ggttagacgt ggcagctctg 700  
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 attctctgg 770

<210> 90

<211> 1229

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (96)...(554)

<400> 90

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Legagttgc atctgagaaa gtgcccaga agaca atg gac tat gtg tgc tgt 113

Met Asp Tyr Val Cys Cys

1

5

gct tac aac aac ata ecc ggc agg caa gat gaa act cat ttc aca gtt 161

Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp Glu Thr His Phe Thr Val

10

15

20

atc atc act tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca 209

Ile Ile Thr Ser Val Gly Leu Glu Lys Leu Ala Gln Lys Gly Lys Ser

25

30

35

ttg tca cct tta gca agt ata act gga ata tca cta ttt ttg att ata 257

Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile Ser Leu Phe Leu Ile Ile

40

45

50

tcc atg tgt ctt ctc ttc cta tgg aaa aaa tat caa ccc tac aaa gtt 305

99/177

Ser Met Cys Leu Leu Phe Leu Thr Lys Lys Tyr Gln Pro Tyr Lys Val  
 55 60 65 70  
 ata aaa cag aaa cta gaa ggc agy cca gaa aca tac agy aaa gct 353  
 Ile Lys Gln Lys Leu Gln Gly Arg Pro Gln Thr Tyr Arg Lys Ala  
 75 80 85  
 caa aca ttc tca ggc cat gaa gat gct ctg gat gac ttc gga ata cat 401  
 Gln Thr Phe Ser Gly His Gln Asp Ala Leu Asp Asp Phe Gly Ile Tyr  
 90 95 100  
 gaa ttt gtc gct ttc cca gat gtc tct gtc gtc tcc agy atc cca agc 449  
 Gln Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser  
 105 110 115  
 agy tct gtc cca gcc tct gat tgt gta tcy ggg caa gat ttg cac agt 497  
 Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser  
 120 125 130  
 aca gtc tat gaa gtc atc cag cac atc cct gcc cag cag caa gac cat 545  
 Thr Val Tyr Gln Val Ile Gln His Ile Pro Ala Gln Gln Asp His  
 135 140 145 150  
 cca gag tgaacttca tgggtcaaac agtcaactcg agtgaatttc tgaagaac 600  
 Pro Gln  
 20  
 atttaagga aaaacagtcgg aaaaattat taatctggaa tcaagtgaa aacaaagac 660  
 aacactctt acatattat cctttcaag cagatagag gcatttatgc aattgaact 720  
 gaagttttt cagcatatc acaatgctt gtgcacaga aaaaatggtt ggggaatat 780  
 tctcagtcgg agagtcgtc tcaatctgac ggggagagc aagtcgacg ggttcctc 840  
 aaaaatttg tatgaatat ctctacaac ctcaattagt tctactctac aattcacta 900  
 tcatcaaac tgaactatc ctgtctaac tacaatgfy gaaacttca atgttcgat 960  
 ttctcagag acattgctt attaatitt tattagctt aagaatgcta aagtttcat 1020  
 ttatttcca aatttctac ttgtatttg taacaaag taatagat gtttcgaca 1080  
 aaaaacaaac tatgcctct ctttttttc aatcacaagt agtatcttg agagactg 1140  
 tgaacttca aggaatgac tactaagtc ttattttat ttttttaag gaagatgga 1200  
 ttcaataaa ttattctgtt ttgtcttt 1229  
 25  
 30  
 35  
 <210> 91  
 <211> 358  
 <212> PRT

100/177

<213> Homo sapiens  
 <400> 91  
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 Ile Gly Ala Val Ile Ala Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val  
 20 25 30  
 Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu  
 35 40 45  
 Ala Leu Gln Leu His Pro Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln  
 50 55 60  
 Gln Lys Phe Gln Asp Leu Gly Ala Ala Tyr Gln Val Leu Ser Asp Ser  
 65 70 75 80  
 Gln Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Gln Gln Gly Leu Lys Asp  
 85 90 95  
 Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Gly Asp  
 100 105 110  
 Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Asn Ile  
 115 120 125  
 Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Gln Val Thr Leu Gln Gln  
 130 135 140  
 Val Tyr Ala Gly Asn Phe Val Gln Val Val Arg Asn Lys Pro Val Ala  
 145 150 155 160  
 Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Gln Met Arg  
 165 170 175  
 Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Gln Val Val  
 180 185 190  
 Cys Asp Gln Cys Pro Asn Val Lys Leu Val Asn Gln Gln Arg Thr Leu  
 195 200 205  
 Gln Val Gln Ile Gln Pro Gly Val Arg Asp Gly Met Gln Tyr Pro Phe  
 210 215 220  
 Ile Gly Gln Gly Gln Pro His Val Asp Gly Gln Pro Gly Asp Leu Arg  
 225 230 235 240  
 Phe Arg Ile Lys Val Val Lys His Pro Ile Phe Gln Arg Arg Gly Asp  
 245 250 255  
 25  
 30  
 35

102/177

Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser  
115 120 125  
Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp  
130 135 140  
5 Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu Ile Ile Leu Leu  
145 150 155 160  
Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val  
165 170 175  
10 Trip Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu  
180 185 190  
Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Pro Tyr Asp  
195 200 205  
Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro Pro Tyr Val  
210 215 220  
15 Ser Ala  
225  
<210> 93  
<211> 195  
20 <212> PRT  
<213> Homo sapiens

<400> 93  
Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg  
1 5 10 15  
Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys  
20 25 30  
Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
35 40 45  
30 Xaa Gly Tyr Arg Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln  
50 55 60  
Arg Tyr Pro Asp Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro  
65 70 75 80  
Ile Tyr Arg His Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu  
85 90 95

101/177

Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly  
260 265 270  
Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser  
275 280 285  
5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu  
290 295 300  
Gly Leu Pro Asn Phe Asp Asn Asn Ile Lys Gly Ser Leu Ile Ile  
305 310 315 320  
Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg  
320 325 330 335  
10 Gly Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr  
340 345 350  
Asn Gly Leu Gln Gly Tyr  
355  
15 <210> 92  
<211> 226  
<212> PRT  
<213> Homo sapiens

<400> 92  
Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys  
1 5 10 15  
Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr  
20 25 30  
Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala  
35 40 45  
Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe  
50 55 60  
30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu  
65 70 75 80  
Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln  
85 90 95  
Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe  
100 105 110



Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met  
 100 105 110  
 Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala  
 115 120 125  
 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met  
 130 135 140  
 Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser  
 145 150 155 160  
 Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile  
 165 170 175  
 Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His  
 180 185 190  
 His Arg Ser  
 195  
 15  
 <210> 94  
 <211> 339  
 <212> PRT  
 <213> Homo sapience  
 20  
 <400> 94  
 Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu  
 1 5 10 15  
 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
 20 25 30  
 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
 35 40 45  
 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
 50 55 60  
 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser  
 65 70 75 80  
 Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu  
 85 90 95  
 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu  
 100 105 110

Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu  
 115 120 125  
 Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg  
 130 135 140  
 Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu  
 145 150 155 160  
 Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His  
 165 170 175  
 Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu  
 180 185 190  
 Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His  
 195 200 205  
 Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr  
 210 215 220  
 Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn  
 225 230 235 240  
 Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn  
 245 250 255  
 Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu  
 260 265 270  
 Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu  
 275 280 285  
 Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp  
 290 295 300  
 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe  
 305 310 315 320  
 Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr  
 325 330 335  
 Lys His Asp  
 30  
 <210> 95  
 <211> 487  
 <212> PRT  
 <213> Homo sapience  
 35

105/177

<400> 95  
 Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys  
 1 5 10 15  
 Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro  
 20 25 30  
 Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val  
 35 40 45  
 Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser  
 50 55 60  
 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu  
 65 70 75 80  
 Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe  
 85 90 95  
 Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu  
 100 105 110  
 Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala  
 115 120 125  
 Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser  
 130 135 140  
 Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu  
 145 150 155 160  
 Ala Ala Val Ala Ala Leu Leu Gly Val Val Ser Arg Glu Glu Val  
 165 170 175  
 Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala  
 180 185 190  
 Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile  
 195 200 205  
 Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile  
 210 215 220  
 Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val  
 225 230 235 240  
 Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu  
 245 250 255  
 Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala  
 260 265 270  
 35

106/177

Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro  
 275 280 285  
 Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser  
 290 295 300  
 5 Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro  
 305 310 315 320  
 Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg  
 325 330 335  
 Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu  
 340 345 350  
 Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser  
 355 360 365  
 Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro  
 370 375 380  
 15 Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser  
 385 390 395 400  
 Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu  
 405 410 415  
 Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu  
 420 425 430  
 Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu  
 435 440 445  
 Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe  
 450 455 460  
 25 Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser  
 465 470 475 480  
 Glu Leu Ala Ser Gly Pro Pro  
 485  
 30 <210> 96  
 <211> 393  
 <212> PRT  
 <213> Homo sapience  
 35 <400> 96

107/177

Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Ala Cys Ser Pro  
 1 5 10 15  
 Val His Thr Thr Leu Ser Ser Ser Asp Ala Lys Lys Ala Ala Ser Lys  
 20 25 30  
 6 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg  
 35 40 45  
 Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Val Leu Glu His  
 50 55 60  
 Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp  
 10 65 70 75 80  
 Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr  
 85 90 95  
 Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln  
 100 105 110  
 15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp  
 115 120 125  
 Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu  
 130 135 140  
 His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe  
 145 150 155 160  
 Arg Asn Val Leu Asp Ser Ser Glu Asp Glu Ile Glu Glu Ser Lys Thr  
 165 170 175  
 Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu  
 180 185 190  
 25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met  
 195 200 205  
 Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu  
 210 215 220  
 Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met  
 225 230 235 240  
 Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe  
 245 250 255  
 Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn  
 260 265 270  
 35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

108/177

275 280 285  
 Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe Tyr Gly Met  
 290 295 300  
 Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu Pro Val Val Gly Ala Arg  
 6 305 310 315 320  
 Tyr Ile Gln Thr Leu Lys Asp His Arg Pro Arg Met Val Trp Asp Ser  
 325 330 335  
 Gln Ala Ser Glu His Phe Phe Glu Tyr Lys Lys Ser Arg Ser Gly Arg  
 340 345 350  
 10 His Val Val Phe Tyr Pro Thr Leu Lys Ser Leu Gln Val Arg Leu Glu  
 355 360 365  
 Leu Ala Arg Glu Leu Gly Val Val Ser Ile Trp Glu Leu Gly Gln  
 370 375 380  
 Gly Leu Asp Tyr Phe Tyr Asp Leu Leu  
 15 385 390  
 <210> 97  
 <211> 196  
 <212> PRT  
 <213> Homo sapiens  
 20  
 <400> 97  
 Met Trp Arg Val Pro Gly Thr Thr Arg Arg Pro Val Thr Gly Glu Ser  
 1 5 10 15  
 Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Thr Leu Ala  
 20 25 30  
 Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro Gly Gly  
 35 40 45  
 Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile Thr Gly  
 50 55 60  
 Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln Val Lys  
 65 70 75 80  
 Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly Asn Thr  
 85 90 95  
 35 Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val Phe Val

109/177

110/177

100 105 110  
Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp  
115 120 125  
Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr  
130 135 140  
Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln  
145 150 155 160  
Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu  
165 170 175  
10 Glu Pro Thr Thr Glu Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser  
180 185 190  
Pro Val Gly Arg  
195

5

15 <210> 98  
<211> 107  
<212> PRT  
<213> Homo sapiens

20 <400> 98  
Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met Ser  
1 5 10 15  
Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly Ser  
20 25 30  
25 Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile  
35 40 45  
Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser  
50 55 60  
Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala  
65 70 75 80  
Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser  
85 90 95  
Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro  
100 105

35

<210> 99  
<211> 350  
<212> PRT  
<213> Homo sapiens  
5  
<400> 99  
Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly Pro Lys Gly Ala Pro  
1 5 10 15  
Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly Lys Thr Pro Val Ala  
20 25 30  
Arg Ser Ser Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser  
35 40 45  
Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln  
50 55 60  
15 Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Lys  
65 70 75 80  
Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile  
85 90 95  
Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser  
100 105 110  
Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Ile Asn Glu  
115 120 125  
Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn  
130 135 140  
25 Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser  
145 150 155 160  
Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys  
165 170 175  
Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu  
180 185 190  
30 Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile Glu Lys Val Glu Lys  
195 200 205  
Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ile Asp Arg  
210 215 220  
35 Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn

111/177

225 230 235 240  
 Ser Val Lys Lys Thr Leu Thr Gln Leu Lys Ser Asp Phe Asp Lys His  
 245 250 255  
 Thr Asp Arg Phe Leu Ser Leu Gln Gly Asp Arg Ala Lys Val Leu Lys  
 260 265 270  
 Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys  
 275 280 285  
 Lys Asp Phe Ser Arg Leu Leu Gln Pro Leu Val Asn Asp Leu Thr Leu Arg  
 290 295 300  
 Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Gln Lys Gln Ile Ala  
 305 310 315 320  
 Phe Leu Ser Gln Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Gln Ile  
 325 330 335  
 Lys Asp Ile Lys Asp Gln Ile Ala His Ile Ser Asp Met Asn  
 340 345 350  
 15  
 <210> 100  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens  
 20  
 <400> 100  
 Met Ser Ser Ala Gly Thr Ala Thr Pro Leu Gln Met Asp His Lys Leu  
 1 5 10 15  
 Thr Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser  
 20 25 30  
 Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Gln  
 35 40 45  
 Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Gln Cys Val  
 50 55 60  
 Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu  
 65 70 75 80  
 Leu Val Val Gly Gln Ala Pro Ala Trp Gln Gly Ser Leu Leu Arg Gly  
 85 90 95  
 35 Arg Pro Ala Gly Ala His Leu Cys Ala Ala

112/177

100 105  
 <210> 101  
 <211> 1074  
 <212> DNA  
 <213> Homo Sapiens  
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 <400> 101  
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 atggcggac gaggattcta taagatctg ggggtgcgc gaagtgcctc tataaagat  
 attaaaaag cctataggaa actagcctg cagcttcatc ccgaccgaa ccatgatgat  
 ccacaaagcc aggaagaatt ccagatctg ggtgcgtct atgaggtctc gtccagatagt  
 gagaagaagg aacagtacga taatttgt gaagaagatc taagaatcgt tcatcagagc  
 tcccatggag acaattttc aaactcttc ggggatttct gtaccatgtc tggaggaacc  
 tccctgcagc aagaacagaa tatccaaag ggaagtga taattgtaga tctagaagtc  
 actttggaag aagtatatgc aggaatttc gtgcgaagtag ttgaacaaca aactgtgcga  
 aggcagagtc ctggcaaaag gaagtgaat tgcgcgaag agatgcggac caaccagctg  
 ggcctcgggc gcttccaatc gaaccaggag gtgtctcgcg acgaatgcctc taatgtcaaa  
 ctagtgaatg aagaacagac gctggaagta gaattagagc ctgggtgtgag agacggcatg  
 gagtaccctc ttattggaga aggtgagctc cagcttgatg gggagcctg agattacgg  
 ttccgaacca aagttgtcaca gaaccaata ttgaaagga gaggagatga ttgtacaca  
 aatgtacaaa tctcattagt tgnatcactg gtgtgcttgg agatggatat taactactg  
 gatgtcaca agtatatatc ttcccgatc agatcacca ggcagggagc gaagctatgg  
 aagaagaagg aaggctccc caacttgac aacacaata tcaagggtcc ttgtatcacc  
 actttgatg tgaatttcc aagaagacag ttaagaagg aagcagaga aggtatcaaa  
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 20 25  
 <210> 102  
 <211> 678  
 <212> DNA  
 <213> Homo Sapiens  
 30  
 <400> 102  
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 gtccgacgg gaccatcct gctcggctc tgaatctga tcatcaatgc tgtgtactg  
 35 60 120

113/177

114/177

5  
10  
15  
20  
25  
30  
35

ttgattttat tgaatgacct ggctgatacc gatacagata accttcaag ttctgaactg 180  
ggaggtgact ttgagtctat ggaatgatcc aacatgta ttgcattgc gatttctt 240  
ctcatgacc tgatagtgc tatggtact taaggagct acaagaacg cgcagctgg 300  
atcatccat tctcttgta ccagatctt gacttgc ttgaatggt ggtgaacac 360  
actgtgta ttatccaa ctccattcag gaatacat ggcacatgcc tctcaattt 420  
ccctacagag atgatgcat gcaatgaat cctactgtt tggctctat tattctctg 480  
ttattagca ttacttgac ttttaaggt tacttgatta gctgtgtt gactgctac 540  
cgatacatca atggttagaa cctctctgat gctatggtt atgtacacg caatgaact 600  
acggtgctgc taaccocgta tgatgatgcc actgtgaatg gtgtgcaa ggaaccacg 660  
ccacttaccg tgtctgcc 678

<210> 103  
<211> 585  
<212> DNA  
<213> Homo Sapience

<400> 103  
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gcaaatcgg gcggctgcc cagcaagaga ttaagatgc agtaagcac ggggcgctg 120  
ctcaagttcc agatttctg tctctgaggt tataggcggg tgttgaggga gtacatggg 180  
gttattagcc agcggtaacc agacatccgc attgaaggg agaatcact cctcaacca 240  
atatatagac acatagcacc ttctctgta gcttcaac tagtattant aggttaata 300  
attgttgca aggtacct ttcttctt ttgcttctt ggcataag cctatagcat ctggcagtgg 360  
ggcaagaaa ataagttta tgcagtatg atggtttct tcttgagcaa catgattgag 420  
accagtgta tgcacacag tgcatttgg ataacittaa atgagtacc tgtgtgctt 480  
aagctgaat ctggtacact tcatccatg caacacttg caacacttg tcaattct tgaacatga 540  
atgaagctea atgtgatat ggaattcaac caacaccacc gata 585

<210> 104  
<211> 1017  
<212> DNA  
<213> Homo Sapience

<400> 104  
atgaactggg agctgtgct gtggtgctg gtgctgtgcg cgtgtcct gctcttggg 60

5  
10  
15  
20  
25  
30  
35

cagctgtgc gcttctgag ggcagcggc gacatgagc tactatgagc cgaatggcag 120  
ggcagcggc aagatggga gctgactgat atggtggtgt gggtagctgg agcctcaggt 180  
ggatgttg agagctggc ttaccagttg tctaaactag ggtttctct tgtgtgta 240  
ggcagagag tgcagtact ggaaggggtg aagaagat gcttagaga tggcaattt 300  
aagaanaag atactctgt ttgcccctt gacatgacg acactgttcc ccatgaagcg 360  
gtccaaag ctgtctoca ggaatttgg agaatgaca ttctgtcaa caatgggga 420  
atgcccagc gttctctg catggatacc agcttgatg tctacagaaa gataatagag 480  
cttaactact taggacggt gctctgaca aaatgtgtc tgcctacat gatcagaggg 540  
aagaagga agattgtac tgtgaatagc atctgggta tcatatctgt acctttcc 600  
attgatact gtgtagcaa gcatgctc cgggttttt ttaatggcct tgaacagaa 660  
cttgccat acctaggat aatgttct acatttgc caggacctgt gcaataaat 720  
attgtgga attcctagc tggagaagtc acaagacta taggaataa tggagaccag 780  
tccacaaga tgacaaccg tegtgtgtg cgtgtgatg taatcagcat ggcataatgt 840  
ttgaagaag ttggatct agacaacct ttctgttg taacatatt gtgcaatgc 900  
atgcaacct gggctgtgtg gataccaa acatggggga agaaaggat tgaacattt 960  
aagtggtg tggatgaga ctcttctat tttaaatct ttaagacaaa acatgac 1017

<210> 105  
<211> 1461  
<212> DNA  
<213> Homo Sapience

<400> 105  
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agggccctg agagcaag cgtgacccc aagcactgg agactgacc tagcagggag 180  
accgctgt ccataggct taagtgacc gtgccttca tgttgccgg cctggagctg 240  
tctggggcg gcatgtctt ggaatttcc cagcactgg ctgtgttctt ggaagtga 300  
gaactttga catgtgccc gacctgtg ggcataag ggaactgga gatgacactg 360  
gataccagc tctccagc tgcaacact ggcaaatg atgacccca ggaagcagc 420  
agagtcaatc gacgaacct ggcctcacc caggtcagg cactgtcgt ggggctcttg 480  
gctgtgtgg ctgcgtgt gttggcgtg gtgtctcag aggaagtga tgcgccag 540  
gtggagttgc tgtgtccag cagtgtctc actgcttcc ttgagcctt tgcctgggg 600  
gtgtgtagg tctgtatgt gattgtgt cgaagctcg ggtgcaacc agacaactt 660  
ggcagccca ttgagccag cctgggagac ctctacac tgccttctt ggttttgtt 720

116/177

agacagcttct tctacagaca caaagataagt cgttatctga cgcgcgtgt ctgcacaga 780  
tttgcggttc tgcacacagat gtggtgtctc attgcacagc agagaccacc catcgtgaag 840  
atctcgaagt ttgtctgtgt cccatcacac ctgcgcacag tcatcagag ttccgtagga 900  
ctcatcttga gcaaacctgt tcttaaacag cagtacaaag gcatggagat attaacccg 960  
gtcatctgt gtgtgtgtgt caatctgtgt gcatcacaga ccaagagat ctcaactac 1020  
ctgcacacgt gtagtgcacc tgggtctcgt cccctcacga tgaagaatt ctggccaac 1080  
ccgtgttcta cttcttgac gtccagaaac aattcacat cagtcgagt cctgccttg 1140  
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gtatataaca gcaagacct tgtgtgttc taactgtgt caggtcgtat ccaagtgaac 1260  
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&lt;211&gt; 1179

&lt;212&gt; DNA

&lt;213&gt; Homo Sapiens

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35

116/177

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5

&lt;210&gt; 107

&lt;211&gt; 588

&lt;212&gt; DNA

&lt;213&gt; Homo Sapiens

10

&lt;400&gt; 107

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&lt;210&gt; 108

&lt;211&gt; 321

&lt;212&gt; DNA

&lt;213&gt; Homo Sapiens

25

&lt;400&gt; 108

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117/177

118/177

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		ctagaaccca atgaattcca acaacttcaa agtaaatca gtttaatttc agaaaagtgg	300
		cagaaatctg aagctatcat ggaacnatty aagtcctttc aataattgc tcaatcaag	360
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		cggatttcag gtttagtaac tgatgata tcaatgacag attctgtgca agaatagaa	600
		aaaaaatag agaaagtga aaaaataca aaaaataca taggtgactc tcttcaagc	660
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		ctaagcttag aagtgacag agccaagtt ctgaagacag tgacttttgc aaatgactca	840
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		Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile	
		25 30 35	
25		aag gat att aaa aag gcc tat agg aaa cta gcc ctg cag ctt cat ccc	319
		Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro	
		40 45 50	
		gac cgg aac cct gat gat cca caa gcc cag gag aaa ttc cag gat ctg	367
		Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Glu Lys Phe Gln Asp Leu	
30		55 60 65 70	
		ggg gct gat gag gtt ctg tca gat agt gag aaa cgg aaa cag tac	415
		Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser Glu Lys Arg Lys Gln Tyr	
		75 80 85	
		gat act tat ggt gaa gaa gga tta aaa gat ggt cat cag agc tcc cat	463
35		Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp Gly His Gln Ser Ser His	



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105 110 115  
gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att 559  
gly thr pro arg gln glu asp arg asn ile pro arg gly ser asp ile  
120 125 130  
att gta gat cta gaa gta cta ttg gaa gaa gta tat gca gga aat ttt 607  
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135 140 145 150  
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val glu val val arg asn lys pro val ala arg gln ala pro gly lys  
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arg lys cys asn cys arg gln glu met arg thr thr gln leu gly pro  
170 175 180  
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val lys leu val asn glu glu arg thr leu glu val ile glu pro  
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gly val arg asp gly met glu tyr pro phe ile gly glu gly glu pro  
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his val asp gly glu pro gly asp leu arg phe arg ile lys val val  
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aag caa cca ata ttt gaa aag aga gga gat gat ttg tac aca aat gtc 943  
lys his pro ile phe glu arg arg gly asp asp leu tyr thr asn val  
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aca atc tca tta gtc gag tca ctg gtc ggc ttt gag atg gat att act 991  
thr ile ser leu val glu ser leu val gly phe glu met asp ile thr  
265 270 275  
cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg 1039

his leu asp gly his lys val his ile ser arg asp lys ile thr arg  
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pro gly ala lys leu tyr lys lys gly glu gly leu pro asn phe asp  
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121/177

122/177

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 Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu  
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 Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln  
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&lt;220&gt;

123/177

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Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Gln Ala Ser  
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Ala Asn Leu Gln Gln Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala  
25 30 35  
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Thr Gln Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gln Tyr Arg  
40 45 50  
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Arg Val Phe Gln Gln Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp  
55 60 65  
atc cgc att gaa gga gag aat tac ctc cct cca cca ata tat aga cac 294  
Ile Arg Ile Gln Gln Gln Asn Tyr Leu Leu Pro Gln Pro Ile Tyr Arg His  
70 75 80  
ata gca tct ttc ctg tca gtc ttc aca cta gta tta ata ggc tta ata 342  
Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gln Leu Ile  
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Ile Trp Gln Trp Gln Gln Gln Asn Lys Val Tyr Ala Cys Met Met Val  
120 125 130  
ttc ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca 486  
Phe Phe Leu Ser Asn Met Ile Gln Asn Gln Cys Met Ser Thr Gln Ala  
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124/177

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Gln His Leu Pro Ser Met Gln Gln Leu Val Gln Ile Leu Asp Asn Gln  
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Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser  
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Met Asn  
1

125/177

126/177

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 Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu  
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 Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp  
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 10 atg gtc gtc tgg gtc act gga gcc tcg agt gga att ggt gag gag ctg 310  
 Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu  
 55 60 65  
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 70 75 80  
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 Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly  
 85 90 95  
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 Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp  
 100 105 110  
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 Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly  
 115 120 125 130  
 25 aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg 550  
 Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu  
 135 140 145  
 tgc atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac 598  
 Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn  
 150 155 160  
 30 tcc tta ggg acg gtc tcc ttg aca aaa tgc gtt ctg cct cac atg atc 646  
 Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile  
 165 170 175  
 gag agg aag caa gga aag att gtt act gtc aat agc atc ctg ggt atc 694  
 Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile

180 185 190  
 ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc 742  
 Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu  
 195 200 205 210  
 5 cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt 790  
 Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly  
 215 220 225  
 ata ata gtt tct aac att tgc cca gga cct gtc caa tca aat att gtc 838  
 Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val  
 230 235 240  
 10 gag aat tcc cta gct gga gaa gtc aca aag act ata ggc aat aat gga 886  
 Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly  
 245 250 255  
 gac cag tcc cac aag atg aca acc agt cgt tgt gtc cgg ctg atg tta 934  
 Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu  
 260 265 270  
 atc agc atg gcc aat gat ttg aaa gaa gtt tgg atc tca gaa caa cct 982  
 Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro  
 275 280 285 290  
 20 ttc ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg 1030  
 Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp  
 295 300 305  
 tgg ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt 1078  
 Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser  
 310 315 320  
 25 ggt gtc gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat 1126  
 Gly Val Asp Ala Asp Ser Tyr Phe Lys Ile Phe Lys Thr Lys His  
 325 330 335  
 gac tgaagagac atctgtactt ttcagccac tggaggaaa aatggaaaac a 1180  
 Asp  
 30  
 35 <210> 115  
 tgaagacagc aatctcttta tgcctctgaa tantcaaga ctaattttgt gtttacttt  
 ttaatgata tgcattttgt tccaacatgg aatgaatatan aaataaagta at 1240  
 1292

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10	tcttcgcacg cgcctggag gggaccggg ctgcacagcg ccacgtgtg ccacg		55
	atg gat ggg aca gag acc cgg cag cgg agg ctg gac agc tgt ggc aag		103
	Met Asp Gly Thr Glu Thr Arg Gln Arg Ala Asp Ser Cys Gly Lys		
	1          5                        10                        15		
	cga ggg gag ctg ggg ctt cct cac ccc ctg agc aca gga gga ctc cct		151
	Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro		
	20                        25                        30		
15	gta gcc tca gaa gat gga gct ctg agg gcc cct gag agc caa agc gtg		199
	Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val		
	35                        40                        45		
	acc ccc aag cca ctg gag act gag cct agc agg gag acc gcc tgg tcc		247
20	Thr Pro Lys Pro Leu Glu Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu		
	50                        55                        60		
	ata ggc ctt cag gtg acc gtg ccc ttc atg ttc gca ggc ctg gga ctg		295
	Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu		
	65                        70                        75                        80		
25	tcc tgg gcc gag atg ctt ctg gac tat ttc aag cac tgg cct gtg ttt		343
	Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe		
	85                        90                        95		
	gtg gag gtg aaa gac ctt ttg aca ttg gtg ccg ccc ctg gtg ggc ctg		391
	Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu		
	100                        105                        110		
30	aag ggg aac ctg gag atg aca ctg gca tcc aga ctc tcc aca gct gcc		439
	Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala		
	115                        120                        125		
	aac act gga caa act gat gac ccc cag gag cag cac aga gtc atc agc		487
35	Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser		

130	135	140	535
agg aac ctg gcc ctc atc cag gtg cag gcc act gtc gtg ggg ctg ttg			
Ser Aan Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu			
145	150	155	160
gct gct gtg gct ggg ctg ctg ttg ggc gtg gtc tct cga gag gaa gtg			
Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Gln Val			
165.	170	175	
ggt gtc gcc aag gtg gag ttg ctg tgt gcc agc agt gtc ctg act gcc			631
Asp Val Ala Lys Val Gln Leu Leu Cys Ala Ser Ser Val Leu Thr Ala			
180	185	190	
ttc ctt gca gcc ttt gcc ctg ggg gtg ctg atg gtc tgt ata gtg att			679
Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile			
195	200	205	
ggt gct cga aag ctg ggg gtc aac cca gac aac att gcc acg ccc att			727
Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile			
210	215	220	
gga gcc agc ctg gga gac ctg atc aca ctg tcc att ctg gct ttg gtc			775
Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val			
225	230	235	240
agg agc ttc ttc tac aga ccc aaa gat agt cgg tat ctg acg ccg ctg			823
Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu			
245	250	255	
gtc tgc ctg agc ttt gcg gct ctg acc cca gtg tgg gtc ctg att gcc			871
Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala			
260	265	270	
aag cag agc cca ccc atc gtg aag atc ctg aag ttt ggc tgg ttc cca			919
Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro			
275	280	285	
atc atc ctg gcc atg gtc atc agc agt ttc gga gga ctg atc ttg agc			967
Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser			
290	295	300	
aaa acc gtc tct aaa cag cag tac aaa gcc atg gag ata ttt acc ccc			1015
Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro			
305	310	315	320
gfc ata tgt ggt gtc ggt gcc aat ctg gtg gcc att cag acc agc cga			1063

129/177

130/177

Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg  
 325 330 335  
 atc tca acc tac ctg cac atg tgg agt gca cct ggc gtc ctg ccc etc 1111  
 Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu  
 340 345 350  
 cag atg aag aaa ttc tgg ccc aac ccc tgt tct act ttc tgc acg tca 1159  
 Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser  
 355 360 365  
 gaa atc aat tcc atg tca gct cga gtc ctg ctc ttg ctg gtc gtc cca 1207  
 Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro  
 370 375 380  
 ggc cat ctg att ttc ttc tac atc atc tac ctg gtc gag ggt cag tca 1255  
 Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser  
 385 390 395 400  
 gtc ata aac agc cag acc ttt gtc gtc ctc tac ctg ctg gca ggc ctg 1303  
 Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu  
 405 410 415  
 atc cag gtc aca atc ctg ctg tac ctg gca gaa gtc atg gtt cgg ctg 1351  
 Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu  
 420 425 430  
 act tgg cac cag ggc ctg gat cct gac aac cag tgc atc ccc tac ctt 1399  
 Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu  
 435 440 445  
 aca ggg ctg ggg gac ctg ctc ggt act ggc etc ctg gca etc tgc ttt 1447  
 Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe  
 450 455 460  
 ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca 1495  
 Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Ile Ser  
 465 470 475 480  
 gaa ctg gca tct gga cct ccc taactgggccc ccgctgtccc catitgtcca ttac 1550  
 Glu Leu Ala Ser Gly Pro Pro  
 485  
 aatttctct cactatngtg ggaacagaa ttcagtttct cccctgacag gtccttggga 1610  
 tggtagcccc ctgcctctgc agtagccttt tgtgagctcg ctaaggtagc tctacacac 1670  
 ctggctctg gggtagatc ctgagctgc aatagagccc tgaatcaag agcatggctt 1730

gegtgtgc atatgtgtg tgcacatgct taatgagcgt gcaagtggtc acacgtttgt 1790  
 ggaagagagg gtgtctggc ctgagaagct aaggaagagg catgtccagt atgctttgca 1850  
 ggggtgttt gctttttcc atgcccacgc aaccacagatt ggggtggagc aggaagagagc 1910  
 tcttttctg tcccaagcct cagaactctt gagctgtggc ttaactgtgtg tcttaccagc 1970  
 5 gttcaagctc cgtgggccc actgctgtgtg tgcacagag gtgtacagcc tcccagagat 2030  
 ggggctcat acacaccttc atctgcctc acatttaast cgtgtccttg ctgtcttttt 2090  
 atttcttt ttgttagcaa aaacctctat tttagtttca ataactagag aagtgtaaaa 2150  
 taaaacagat tatattgt 2168

10 &lt;210&gt; 116

&lt;211&gt; 1357

&lt;212&gt; DNA

&lt;213&gt; Homo Sapiens

&lt;220&gt;

15 &lt;221&gt; CDS

&lt;222&gt; (81)...(1262)

&lt;400&gt; 116

cgtggtttg tggcgttcg gctcctcga catgagccc tctgacccc gaggttgagc 60  
 cctactgtga caccactaac atg cgg aca etc ttc aac etc etc tgg ctt 110  
 Met Arg Thr Leu Phe Asn Leu Leu Trp Leu  
 1 5 10

gcc ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc 158  
 Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala

25 15 20 25  
 aaa aaa gcc gcc tca aag acg ctg gag aag agt cag ttt tca gat  
 Lys Lys Ala Ala Ser Lys Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp

30 30 35 40  
 aag cctg gtc cna gac cgg ggt ttg gtc agc gac etc aaa gct gag  
 Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Glu

35 45 50 55  
 agt gtc gtt ctt gag cat cgc agc tac tgc tgc gca aag gcc cgg gac  
 Ser Val Val Leu Glu His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp

35 60 65 70  
 aga cac ttt gct ggg gat gta ctg ggc tat gtc act cca tgg aac agc

131/177

Arg His Phe Ala Gly Asp Val Leu Gly Tyr Val Thr Pro Trp Asn Ser  
75 80 85 90  
cat gag tac gat gtc acc aag gtc ttt ggg agc aag ttc aca cag atc  
His Gly Tyr Asp Val Thr Lys Val Phe Gly Ser Lys Phe Thr Gln Ile  
5 95 100 105  
tca ccc gtc tgg ctg cag ctg aag aga cgt ggc cgt gag atg ttt gag  
Ser Pro Val Trp Leu Gln Leu Lys Arg Arg Gly Arg Gln Met Phe Gln  
110 115 120  
gtc aag ggc ctg ccc gac gtc gac caa ggg tgg atg cga gct gtc aag  
Val Thr Gly Leu His Asp Val Asp Gln Gly Trp Met Arg Ala Val Arg  
125 130 135  
aag cat gcc aag ggc ctg cac ata gtc cct cgg ctg ctg ttt gag gac  
Lys His Ala Lys Gly Leu His Ile Val Pro Arg Leu Leu Phe Gln Asp  
140 145 150  
tgg act tac gat gat ttc cgg aac gtc tta gac agt gag gat gag ata  
Trp Thr Tyr Asp Asp Phe Arg Asn Val Leu Asp Ser Gln Asp Gln Ile  
155 160 165 170  
gag gag ctg agc aag acc gtc gtc cag gtc gca aag aac cag cat ttc  
Gln Gln Leu Ser Lys Thr Val Val Gln Val Ala Lys Asn Gln His Phe  
175 180 185  
gat ggc ttc gtc gtc gag gtc tgg aac cag ctg cta agc cag aag cgc  
Asp Gly Phe Val Val Gln Val Trp Asn Gln Leu Leu Ser Gln Lys Arg  
190 195 200  
gfg ggc ctg atc ccc atg ctg acc ccc ttg ggc gag gct ctg ccc cag  
Val Gly Leu Ile His Met Leu Thr His Leu Ala Gln Ala Leu His Gln  
205 210 215  
ggc cgg ctg ctg ggc ctg ctg gtc atc ccg cct ggc atc acc ccc ggg  
Ala Arg Leu Leu Ala Leu Leu Val Ile Pro Pro Ala Ile Thr Pro Gly  
220 225 230  
acc gac cag ctg ggc atg ttc aag ccc aag gag ttc gag cag ctg ggc  
Thr Asp Gln Leu Gly Met Phe Thr His Lys Gln Phe Gln Gln Leu Ala  
235 240 245 250  
ccc gtc ctg gat gat ttc agc ctg acc atg acc tac gac tac ttc aca ggc  
Pro Val Leu Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala  
255 260 265

132/177

cat cag cct ggc cct aat gca ccc ctg tcc tgg gtc cga gcc tgc gtc  
His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Lys Val  
270 275 280  
cag gtc ctg gac ccg aag tcc aag tgg cga agc aaa atc ctg ggg  
Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly  
285 290 295  
ctc aac ttc tat gct atg gac tac ggc acc tcc aag gat gcc cgt gag  
Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Gln  
300 305 310  
cct gtc gtc ggg gcc aag tac atc cag aca ctg aag gac ccc acc  
Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro  
315 320 325 330  
cgg atg gtc tgg gag agc cag gcc tca gag cac ttc ttc gag tac aag  
Arg Met Val Trp Asp Ser Gln Ala Ser Gln His Phe Phe Gln Tyr Lys  
335 340 345  
aag agc cgc agt ggg aag cac gtc gtc ttc tac cca acc ctg aag tcc  
Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser  
350 355 360  
ctg cag gtc cgg ctg gag ctg gcc cgg gag ctg ggc gtc ggg gtc tct  
Leu Gln Val Arg Leu Leu Gln Leu Ala Arg Gln Leu Gly Val Val Ser  
365 370 375  
atc tgg gag ctg ggc cag ggc ctg gac tac ttc tac gac ctg ctg t  
Ile Trp Gln Leu Gly Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu  
380 385 390  
aggtggacat tgcgcctcc gcggtggagc tgcctcttc taagccatgg agtgagtgag  
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210> 117  
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<213> Homo Sapiens  
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133/177

134/177

&lt;400&gt; 117

aaagcg atg tgg agg gtc ccc gcc aca ace aga cgc cca gtc aca gcc  
Met Trp Arg Val Pro Gly Thr Thr Arg Arg Pro Val Thr Gly

49

1 5 10

gag agc cct ggg atg cac cgg cca gag gcc atg ctg ctg ctg etc acg  
Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Thr

97

15 20 25 30

ctt gcc ctc ctg ggg gcc ccc acc tgg gca ggg aag atg tat ggc cct  
Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro

145

35 40 45

gga gga gcc aag tat ttc agc acc act gaa gac tac gac cat gaa atc  
Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile

193

50 55 60

aca ggg ctg cgg gtc tct gta ggt ctt ctc ctg gta aaa agt gtc cag  
Thr Gly Leu Arg Val Ser Val Gly Leu Leu Val Lys Ser Val Gln

241

65 70 75

gtg aaa ctt gga gac tcc tgg gac gtc gta aaa ctg gga gcc tta ggt ggg  
Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly

289

80 85 90

aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc  
Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val

337

95 100 105 110

ttt gtc gcc ttc caa gct ttc ctc cgg ggt atg gtc atg tac acc agc  
Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser

385

115 120 125

aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct  
Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser

433

130 135 140

gcc tac ccc agc caa gag ggg cag gtc gtc ggc atc tat ggc cag  
Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln

481

145 150 155

tat caa ctc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca  
Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro

529

160 165 170

cta gag gag ccg acc act gag cca cca gtt aat ctc aca tac tca gca

577

Leu Glu Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala

175 180 185

aac tca ccc gtc ggt cgc taggtgggg tatggggcca tccgagctga ggcca  
Asn Ser Pro Val Gly Arg

630

195

tctgtgggt ggtggctgat ggtactggag taactgagtc gggacgtga atctgaatcc  
accaataaat aaagctcttg c

690

711

&lt;210&gt; 118

&lt;211&gt; 651

&lt;212&gt; DNA

&lt;213&gt; Homo Sapience

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (242)...(565)

&lt;400&gt; 118

aaagaacaa gccgggggac tgcagaccag ggaactcggc cgcggggcgg gaagaagtgg  
ggcagcgtt gccagggccg aaaggacttt ggggtgggg gctgggagtc cgtgtctga

60

120

180

240

286

g atg gag cag aag ctt gtc gag gag att ctt caa gca atc act atg  
Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met

1 5 10 15

tca aca gac aca ggt gtt tcc ctt cct tca tat gag gaa gat cag gga  
Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly

334

20 25 30

tca aaa ctc att cga aaa gct aaa gag gca cca ttc gta ccc gtt gga  
Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly

382

35 40 45

ata ggg ggt ttt gca gca att gtt gca tat gga tta tat aaa ctg aag  
Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys

430

50 55 60

agc agg gga aat act aaa atg tcc att cat ctg atc cac atg cgt gtc  
Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val

478

35



65 70 75  
gca gcc caa gcc ttt gtt gta gga gca atg act ggt atg ggc tat 526  
ala ala gln gly phe val val gly ala met thr val gly met gly tyr  
80 85 90 95  
tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa 570  
ser met tyr arg glu phe trp ala lys pro lys pro  
100 105  
ggagatgctgt cctggcctctg ctggagagagc ttgctttcgt tagatgtctt attactaag  
ttacctatta ttgttgaaa t 630  
651  
10  
<210> 119  
<211> 1310  
<212> DNA  
<213> Homo Sapiens  
<220>  
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<222> (78)...(1130)  
15  
<400> 119  
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tccctgggtc tccagac atg tct gag gty aag agc cgg aag tgg ggg 60  
met ser glu val lys ser arg lys lys ser gly 110  
1  
5 10  
ccc aag gga gcc cct gct gcg gag ccc ggg aag cgg agc gag ggc ggg 158  
pro lys gly ala pro ala ala glu pro gly lys arg ser glu gly gly  
15 20 25  
aag aac ccc gtc gcc cgg agc agc gga gcc ggg ggc tgg gca gac ccc 206  
lys thr pro val ala arg ser ser gly gly gly trp ala asp pro  
30 35 40  
cga acg tgc ctg agc ctg ctg tgg ggg aag tgc ctg ggc ctg gcc 254  
arg thr cys leu ser leu leu ser leu gly thr cys leu gly leu ala  
45 50 55  
tgg ttc gta ttc cag cag tca gaa aaa ttc gca aag gtc gaa aac caa 302  
trp phe val phe gln gln ser glu lys phe ala lys val glu asn gln  
60 65 70 75

tac cag tta ctg aaa cta gaa acc aat gaa ttc caa caa ctt caa agt 350  
tyr gln leu leu lys leu glu thr asn glu phe gln gln leu ser  
80 85 90  
aaa atc agt tta att tca gaa aag tgg cag aaa tct gaa gct atc arg 398  
lys ile ser leu ile ser glu lys trp gln lys ser glu ala ile met  
95 100 105  
gaa caa ttg aag tct ttt caa ata att gct cat cta aag cgt cta cag 446  
glu gln leu lys ser phe gln ile ile ala his leu lys arg leu gln  
110 115 120  
gaa gaa att aat gag gta aaa act tgg tcc aat agg ata act gaa aaa 494  
glu glu ile asn glu val lys thr trp ser asn arg ile thr glu lys  
125 130 135  
cag gat ata ctg aac aac agt ctg acg acg ctt tct caa gac att aca 542  
gln asp ile leu asn asn ser leu thr thr leu ser gln asp ile thr  
140 145 150 155  
aaa gta gac caa agt aca act tcc atg gca aaa gat gtt ggt ctg aag 590  
lys val asp gln ser thr thr ser met ala lys asp val gly leu lys  
160 165 170  
att aca agt gta aaa aca gat ata cga cgg att tca ggt tta gta act 638  
ile thr ser val lys thr asp ile arg arg ile ser gly leu val thr  
175 180 185  
gat gta ata tca ttg aca gat tct gtc caa gaa cta gaa aat aca ata 686  
asp val ile ser leu thr asp ser val gln glu leu leu lys ile  
190 195 200  
gag aaa gta gaa aaa aat aca gta aaa aat ata ggt gat ctt tca 724  
glu lys val glu lys asn thr val lys asn ile gly asp leu leu ser  
205 210 215  
agc agt att gat cga aca gca acg ctg cga aag aca gca tct gaa aat 782  
ser ser ile asp arg thr ala thr leu arg lys thr ala ser glu asn  
220 225 230 235  
tca caa aga att aac tct gtt aag aag acg cta acc gaa cta aag agt 830  
ser gln arg ile asn ser val lys lys thr leu thr glu leu lys ser  
240 245 250  
gac ttc gac aaa cat aca gat aga ttt cta agc tta gaa ggt gac aga 878  
asp phe asp lys his thr asp arg phe leu ser leu glu gly asp arg 35

137/177

138/177

255

260

265

gcc aaa gtt ctg aag aca gtg act ttt gca aat gat cta aca cca aag

926

Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys

270

280

5 gtc tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat

974

Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn

285

290

295

gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta cca aga

1022

Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg

300

310

315

gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata

1070

Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile

320

325

330

gtc caa gct gag att aag gat att aag gat gaa ata gca ccc att tca

1118

Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser

335

340

345

gat atg aat tagttgaca ttattgagat tagactaagg taatttttt aat

1170

Asp Met Asn

350

20 gggacctctc atgagaagc tggtaataca aaaaataga tattttgag caaaatcat

1230

tttatatta atctatttt gtacagtaaa aataaaactt taacaacagt tgattttoca

1290

aaataaatat gctaaaacct

1310

&lt;210&gt; 120

&lt;211&gt; 1400

&lt;212&gt; DNA

&lt;213&gt; Homo Sepience

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (233)...(556)

30

&lt;400&gt; 120

tggtgtatg ctattggagg gtggaaatca catctctgt ttatcogtgt gcttattagg

60

tgtcagcgc cccccccc coatatgcag attactcgg catgtatgtg gccagcttct

120

aacacagctg gtatttaag tctctcggga cctcactcag gaatgatccc cctcagtag

180

35

aagcagcagg tgatctaac tcccttcaaa gacagagcct gtcctgggaag cc atg

235

Met

1

tcc tca gca ggc aca gca acc cct ctg gaa atg gat cac aaa ctc act

283

Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu Thr

5

10

15

tct cag cca ggc agc cca agc ttc tat tgt aac agt agc ctc agt ata

331

Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile

20

25

30

gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tgc

379

Val Gly Ser Ser His Gln Leu Gly Phe Thr Phe Ser His Leu Glu Ser

35

40

45

tct gga cta aag gtc ttt cag gtc tcc ttg ccc tgt gag tgc gtc aac

427

Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val Asn

50

55

60

65

ctc ccc acc cga att gcc tca gtt gtc ctg agc ctc atg tct ctc ctg

475

Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu

70

75

80

gtg gtg ggc cag gcc cct gca tgg gaa ggg agc ctg ctg cgg ggc agg

523

Val Val Gly Gln Ala Pro Ala Trip Glu Gly Ser Leu Leu Arg Gly Arg

85

90

95

cca gct ggg ggt gct ccc cta tgc gca gca tgaagtatt gaaggac

570

Pro Ala Gly Gly Ala His Leu Cys Ala Ala

100

105

25 tggttgtga tggtgtgag cgtatcttctc atggcagcg cgaagtgcgc caggtcagcc

630

aggtgcgc agcgtctct ctgcgacttg tctctctg cccagggacc gtggagaag

690

tgtcaggggc cgtcactgc agcagctgc tctctgctt tccctggcag tggtctggg

750

gtggttccc tacactaga tggtcaaggc ctacttttc ctccacaaa ggaagtgcag

810

cccagctagc tctgactgc cactgaca aagtcaagt agcaggtcta ggaagact

870

gggcaatga gcagaggaga cggactctg agctgacca cgaaggcagc cctcactc

930

tggtgggccc tggtcctggt ccttaggtt tgctcaggtg tctctgttg gactcaca

990

ctagtgata agcactggag ggggagacc cgcctggac gtgtttcttt aacctcacc

1050

atataatgg gccgtgggat ggtgtgtag gtaaacagg atgatggtgt tttaagacca

1110

gagctggga cccgggtccc tacactaat ttctctct ggtagctgaa caaaggtcta

1170

aattagctta acaaaagac aggtgcgt cagccagagt tctgaaggcc atgctttg

1230

139/177

tttcctctgt tgcacattgc tctccagttc ctatgaagac aacagagcct agggggcctg 1290  
gcaacagac aacacacac tgggcctgag ctgtgaagag cagggggttg tgcctctgtc 1350  
ctgttctct gcttgcgaa ctcttccaat aacacctact tctatttat 1400

5 <210> 121  
<211> 483  
<212> PRT  
<213> Homo sapience

10 <400> 121  
Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly Ser  
1 5 10 15  
Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Asp Ile Val  
20 25 30  
Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp  
15 35 40 45  
Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu  
50 55 60  
Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly  
20 65 70 75 80  
Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro  
85 90 95  
Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser  
100 105 110  
Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His  
115 120 125  
Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr  
130 135 140  
Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn  
145 150 155 160  
Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu  
165 170 175  
Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr  
180 185 190  
Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

140/177

195 200 205  
Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg Phe  
210 215 220  
Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro  
5 225 230 235 240  
Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp Met  
245 250 255  
Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu  
260 265 270  
Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro Lys  
10 275 280 285  
Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Ser Leu Ala Ile Leu Ser Glu  
290 295 300  
Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe  
15 305 310 315 320  
Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp Gln  
325 330 335  
Phe Ser Gly Pro Lys Ile Met Gln Glu Gly Gln Pro Leu Lys Leu  
340 345 350  
Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser  
20 355 360 365  
Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met Asn  
370 375 380  
Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg  
25 385 390 395 400  
Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu Asn  
405 410 415  
Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser Arg  
420 425 430  
Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu Glu  
30 435 440 445  
Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg Glu  
450 455 460  
Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys Val  
35 465 470 475 480

142/177

210 215 220  
 Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly  
 225 230 235 240  
 Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile  
 245 250 255  
 Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly  
 260 265 270  
 Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile  
 275 280 285  
 Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Val Asn Gln Leu  
 290 295 300  
 His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu Ala His Lys  
 305 310 315 320  
 Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe Cys  
 325 330  
 15  
 <210> 123  
 <211> 267  
 <212> PRT  
 <213> Homo sapiens  
 20  
 <400> 123  
 Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly  
 1 5 10 15  
 His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp  
 20 25 30  
 Thr Glu Leu Arg Gln Trp Glu Gln Gly Glu Leu Leu Leu Pro Leu  
 35 40 45  
 Thr Phe Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val  
 50 55 60  
 Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Glu  
 65 70 75 80  
 Glu Leu Lys Glu Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu  
 85 90 95  
 Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His  
 35

141/177

Lys Ala Met  
 <210> 122  
 <211> 334  
 <212> PRT  
 <213> Homo sapiens  
 5  
 <400> 122  
 Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg Arg Leu Gln  
 1 5 10 15  
 Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu  
 20 25 30  
 Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu  
 35 40 45  
 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro  
 50 55 60  
 Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp  
 65 70 75 80  
 Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu  
 85 90 95  
 Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val  
 100 105 110  
 Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe  
 115 120 125  
 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu  
 130 135 140  
 Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu  
 145 150 155 160  
 Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly  
 165 170 175  
 Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu  
 180 185 190  
 Asp Ala Arg Pro Gly Ser Phe Thr Thr Leu Leu Arg Asn Arg Lys Gly  
 195 200 205  
 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe  
 35

100 105 110  
Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro  
115 120 125  
Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val  
130 135 140  
Tyr Leu Ala Leu Glu Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala  
145 150 155 160  
Trp Ser Gly Leu Arg Phe Phe Glu Pro Trp Gly Leu Trp Leu Arg Ser  
165 170 175  
10 Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Ser Leu Phe Ser Leu  
180 185 190  
Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn  
195 200 205  
15 Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg  
210 215 220  
Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala  
225 230 235 240  
His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala  
245 250 255  
20 Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val  
260 265  
25 <210> 124  
<211> 106  
<212> PRT  
<213> Homo sapience  
30 <400> 124  
Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu  
1 5 10 15  
Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro  
20 25 30  
Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly  
35 40 45  
35 Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser

50 55 60  
Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Glu Met  
65 70 75 80  
Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu  
85 90 95  
5 Gln Asn Pro Glu Pro Met Thr Pro Pro Trp  
100 105  
10 <210> 125  
<211> 224  
<212> PRT  
<213> Homo sapience  
15 <400> 125  
Met Thr Leu Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro  
1 5 10 15  
Tyr Phe Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe  
20 25 30  
Trp Lys Cys Val Glu Ala Gly Val Thr Tyr Leu Phe Val Glu Leu Cys  
35 40 45  
20 Lys Met Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Ile  
50 55 60  
Tyr Asp Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp  
65 70 75 80  
25 Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu  
85 90 95  
Tyr Lys Ile Met Val Ala Ala Leu Glu Tyr Trp Ala Thr Ala Glu Leu Ile  
100 105 110  
30 Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe  
115 120 125  
Asp Trp Lys Tyr Ile Glu Met Ser Ile Asp Ser Asn Ile Ser Leu Val  
130 135 140  
His Tyr Ile Val Ala Ser Ala Glu Val Trp Met Ile Thr Arg Tyr Asp  
145 150 155 160  
35 Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Met Phe Leu Ser

145/177

5 val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu 165 170 175  
180 185 190  
Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu 195 200 205  
Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser 210 215 220  
225  
<210> 126  
<211> 258  
<212> PRT  
<213> Homo sapience

10

<400> 126  
Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg 1  
1 5 10 15  
Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu 20 25 30  
Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly 35 40 45  
Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg 50 55 60  
Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn 65 70 75 80  
Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly 85 90 95  
Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu 100 105 110  
Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp 115 120 125  
Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu 130 135 140  
Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg 145 150 155 160  
Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr 165

20

25 Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly 85 90 95  
Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu 100 105 110  
Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp 115 120 125  
Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu 130 135 140  
Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg 145 150 155 160  
Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr 165

35

146/177

5 Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Trp Thr Phe 195 200 205  
Ser Glu Glu Asn Val Ile Arg Glu Phe Asn Leu Asn Glu Leu Tyr Gln 210 215 220  
Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Glu Glu Gln 225 230 235 240  
Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Glu Asn Lys Lys 245 250 255  
Asp Lys

10

<210> 127  
<211> 110  
<212> PRT  
<213> Homo sapience  
<400> 127  
Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro Pro Phe Ile Ser Glu 1 5 10 15  
Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser 20 25 30  
Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly 35 40 45  
Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu 50 55 60  
Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn Lys Tyr Phe Lys Ser 65 70 75 80  
Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly Gly Leu Phe Thr Tyr 85 90 95  
Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr 100 105 110  
<210> 128

20

35 <210> 128

147/177

<211> 91  
 <212> PRT  
 <213> Homo sapiens  
 5 <400> 128  
 Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser  
 1 5 10 15  
 Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu  
 20 25 30  
 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys  
 35 40 45  
 Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Gly Arg  
 50 55 60  
 Gly Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu  
 65 70 75 80  
 Arg Gly Pro Ser Pro Pro Met Ala Gly Gly  
 85 90  
 <210> 129  
 <211> 344  
 <212> PRT  
 <213> Homo sapiens  
 25 <400> 129  
 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Tyr Ala Pro Leu Ser  
 1 5 10 15  
 Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu  
 20 25 30  
 Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val  
 35 40 45  
 Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys  
 50 55 60  
 Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe  
 65 70 75 80  
 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu  
 35

148/177

85 90 95  
 Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Glu  
 100 105 110  
 Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser  
 115 120 125  
 Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser  
 130 135 140  
 Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr  
 145 150 155 160  
 Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly  
 165 170 175  
 Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys  
 180 185 190  
 Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Lys Ile Pro Ser  
 195 200 205  
 Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser  
 210 215 220  
 Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp  
 225 230 235 240  
 Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe  
 245 250 255  
 Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gly Gly Met  
 260 265 270  
 Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val  
 275 280 285  
 Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu  
 290 295 300  
 Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg  
 305 310 315 320  
 Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val  
 325 330 335  
 Ala Thr Asn Phe Leu Leu Gln His  
 340  
 35 <210> 130

149/177

&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapience

5

Met Gly Pro Pro Gly Ala Gly Val Ser Cys Arg Gly Gly Cys Gly  
1 5 10 15

Phe Ser Arg Leu Leu Ala Trp Cys Phe Leu Leu Ala Leu Ser Pro Gln  
20 25 30

10 Ala Pro Gly Ser Arg Gly Ala Gly Ala Val Trp Thr Ala Tyr Leu Asn  
35 40 45

Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Gly  
50 55 60

Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val  
65 70 75 80

15 Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys  
85 90 95

Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val  
100 105 110

20 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Cys Thr Phe  
115 120 125

Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val  
130 135 140

25 Ile Phe Asn Phe Pro Gly Thr Arg Asn Glu Val Ile Pro Met Ser His  
145 150 155 160

Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly  
165 170 175

Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val  
180 185 190

30 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile  
195 200 205

Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly  
210 215 220

35 Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln  
225 230 235 240

150/177

Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly  
245 250 255

Arg Leu Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Glu Ile Gly Pro  
260 265 270

5 Asp Gly Asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp  
275 280 285

Leu Val Arg Ile Leu Thr Cys Asn-His Ile Phe His Lys Thr Cys Val  
290 295 300

Asp Pro Trp Leu Leu Glu His Arg Thr Cys Pro Met Cys Lys Cys Asp  
305 310 315 320

10 Ile Leu Lys Ala Leu Gly Ile Glu Val Asp Val Glu Asp Gly Ser Val  
325 330 335

Ser Leu Gln Val Pro Val Ser Asn Glu Ile Ser Asn Ser Ala Ser Ser  
340 345 350

15 His Glu Glu Asp Asn Arg Ser Glu Thr Ala Ser Ser Gly Tyr Ala Ser  
355 360 365

Val Gln Gly Thr Asp Glu Pro Pro Leu Glu Glu His Val Gln Ser Thr  
370 375 380

20 Asn Glu Ser Leu Gln Leu Val Asn His Glu Ala Asn Ser Val Ala Val  
385 390 395 400

Asp Val Ile Pro His Val Asp Asn Pro Thr Phe Glu Glu Asp Glu Thr  
405 410 415

Pro Asn Gln Glu Thr Ala Val Arg Glu Ile Lys Ser  
420 425

25

&lt;210&gt; 131

&lt;211&gt; 1449

&lt;212&gt; DNA

&lt;213&gt; Homo sapience

30

&lt;400&gt; 131

etgaagact tccacacttt ctgtgtgtc ctctgtgtt ttggagtggt ctctgaagcc  
eagtttgatg attttgagga tgaggaggac atagtagagt atgatgataa tgacttcgct  
gaatttgagg atgtcatgga agactctgtt actgaatctc ctcaacgggt cataatcct

gaagatgatg aagatgagac cactgtggag ttggaggggc aggatgaaca ccaagaagga

60

120

180

240



15/177

gattttgaag atgcagataac ccaaggagagg gatactgaga gtgaaccata tgaatgana 300  
gaatttgaag gtatagaaga caaacagat acctcttca gnaaaataa agaaccaata 360  
acgatitggt atgttcctgc acacctccag aacagctgg agatitatta tctagaatt 420  
ttgatgtgga ctgtctctgc tgcctataac atgaattaca tcaattgggaa gaataaaac 480  
agtcgccttg ccaagagcttg gtttaacct cacaaggagc ttctggagag caactttact 540  
ttagtggggg atgatggaa taacaaagaa gcaacaaagca caggaaaggt gaacaaagag 600  
aatgaagaca tctataacct gtgtgttat gtgcagagt gtctggaggg catgtttac 660  
cagctgaagt tccctaaagg acaagactta ctgaatgttc tggcccgat gatgaagaca 720  
gtgaatgtac aagtgcaaat aaaaftaac atgaatgttg aagaatgaga taactactga 780  
ttgcgtcttg gcaacagaaa agcctctgtg cgaataagaa aagaatgaga gaatttgaat 840  
gaatttttga gtgataaac taagtctgga gcaaatgttg gaatgcagg ctcttgggc 900  
atcctgtcag agatgggaga agtcacagac gaaatgagt atacaagat gtttcaatt 960  
cttacaacct atgcctgaaa gattgaact gtcaatttt cagacagagt ctctgttcca 1020  
aaaattatgc aagaagaaag taagcttca aagtaacctg acaataagag gaacatgttg 1080  
tttaacttta atgtgccttg ctcaaggtaacctaac aagatgtga ggcactgtta 1140  
cccttgatga acatgttgt ttacttact gataaagca aaaafttccg actcaacaga 1200  
gaaggaacac aaaaagcaga taagaacctg gcccggtag aagaagaact ctgtgaactg 1260  
aacatgtgc aagaacagaa agcagacagc tctcggcgg agagaaaaaa aagaagagag 1320  
aagaagcaga tcaatgaatga ggaagatctc gagaacaagc gaagctgga ggaagtga 1380  
ttggagcttg agaaaagaa gttggaaag aagcaatga aatgaacaa aatcaaatgt 1440  
aaagcatgt 1449

<210> 132  
<211> 1002  
<212> DNA  
<213> Homo sapiens

<400> 132  
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ctctctgtta caagttcttg gctcctact gtccgtgatg cggcttggtg gtatctggac 180  
cgaagaaagc caagcagggg gggccgggac atccagagca taagtgtctg gaactatgg 240  
aagtaacatga aagaaatatt cccactctg ctgttcagaa ctgtctgagct ggaacctct 300  
cgaatacaca ttggggctt ccaacctat ggaatcttg cagtccgagc ctcttgcaac 360  
ctgtgcaactg aagaacaggc ctctctctg atcttcccg gtaaccggcc ccaatctgtg 420

152/177

atgtctgaact tgtgttccg gggccctctc ttcaagagatt acaatcatgtc tgaagggttg 480  
gtcacatcag aaaaaggagag tgtgttcaac attctgaaac ggaagggttg cgaataactg 540  
ctgggcatca ttgtgggggg tggccagagg ggcctgagt ccaagctctg atctttacg 600  
ctgttaactgc ggaacagaaa gggcttctgc aggtccgccc tgaacacgg ggcacacctg 660  
gtgcacatct tccctctcg ggaagatgac ctaattgac agatccaaa ctcttatgc 720  
tccgtgttgc gctatacca gaaatcgttg cagaagatca tgggcatctc acctccacct 780  
tttaatgtgc gtgtgttctt ccagtacagc ttgtgtttaa taacctacg ccggccatc 840  
aacactgttg tgggagagac catcgagta cagaagagagc tgaatccctc ggaaggagag 900  
gtgaacagac tgaacagagc ttatacaca gaagtgtgca acctcttcca ggcacacaaa 960  
cttaagtta acctccctgc tgaacagac ttggaatttc gc 1002

<210> 133  
<211> 801  
<212> DNA  
<213> Homo sapiens

<400> 133  
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caaggggagag tgcctctgc cctaaccttc ctgtactcgg tgcctgggctc cctgtctctc 180  
taactcgttg tgcatacat ggaaccttgc taagtgaatg tgaagcccca gctcaagag 240  
gaatcaagag aagaagcagac agcatgtgt ccttcagaca tccctctcg gtcgtcaga 300  
taactgtctg tgcctagac cctgaaggct cggacatgac gtaagtgcgg ccgttggtc 360  
cggcgttaag acaaacactg cctctgagt gaaatctgtg tgggagagag caaacaccca 420  
ctctttgttg ttaacttgc gctgaagctg gtgtgtcttc tftggggct gtactgtgca 480  
tgttcagagc tccgtttctt ccaagcttg gtctctgtgt tgggttcag cgggtctctg 540  
ttgcgcaact tccgtgtct gtccctcttc tggttgttg ccagctgtct cctgtctcg 600  
caactctaac tgggtggcag caaacacac acctgggaat tcaatccctc acaacgcatc 660  
gcaatactcc gcaagagcgc cagaaacctc ttcaagcagg gactgaaagc caactgtgac 720  
caacttctct gtgtatgagc ctcaaggttc tgggagacc tctgggttga ggaaggagaa 780  
gaaggagaga gcccaagtgt t 801

<210> 134  
<211> 318  
<212> DNA

153/177

164/177

&lt;211&gt; Homo sapiens

&lt;400&gt; 134

5 atgtccacta acatatgtc ggaaccacgg aggcggaaca agtgcgtgag gtacaaagccc 60  
ccgcgaggg aatyaaccc ggccttggaac gaaccgaagc cggactaat gaactcgtg 120  
ggcatgatc taaagatgtg cggactcgtg attaaagtga agtgggtgtg ttgggtcgt 180  
gtactcgtt ccttcataag ctttgcaaac tctggagcgt cggaggaac gaacaaatg 240  
atgtagtagt tcatgtgtc catctctgac gtgggtgatgt cctatctgca gaactctag 300  
cccatgaagc cccatggt 318

10

&lt;210&gt; 135

&lt;211&gt; 672

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

15

&lt;400&gt; 135

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tacaagtga cggcctgtgc cgaataaac gctctctgga aatggtcca ggtcgtggtc 120  
acctacctt ttgtccaaact ctgaagatg ctgtctctgg ccacttctt tccacctgg 180  
gaaggcgca tctatgactt catggggag ttcataaggg ccagcgtgga tgtggagac 240  
ctgataggtc taacctctgt catgtcccg aatgcggca agggagagta caagatcatg 300  
gttctgccc tgggtgggc cactgctgag ctattatgt cccgtcgtat tccctatgg 360  
gtcggagccc ggggcattga gttgactgg aagtaacac agatgagcat agactcaac 420  
atcagctctg tccattacat cgtcgtctct gctcaggtct ggtatgatac acgctatgat 480  
ctgtacaaca ccttcggcc agctgtctc ctgctgatgt tctcagtgct ctacaaggcc 540  
tttattatgg agacctctgt ccaactctgc tgcgtggga gttggcagc tctactggcc 600  
cgagcagtggt taacggggct gctggccctc agcaacttgg cctgtatgt cgcgtgtgc 660  
aatgtgcact cc 672

30

&lt;210&gt; 136

&lt;211&gt; 774

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

35

&lt;400&gt; 136

atgttttaca tctcgaacgg acaagtgtg gacagccgga gtcagctccc atggagatta 60  
tcttgataa cagatttctt ctggggaata gctgagtttg tggttttgt ttccaaact 120

atggcgtct tggcactctt aattgtctc gtgtattcgg tgcgagact ttcaagatgg 60  
ctgcacaaac ctactacct tctgtggcc ctgtctcttg ctgccttctt actcgtgagg 120  
aaactgcgc cgtctgtcca cgtctgccc acccaacggg aagacggtaa cccgtgtgac 180  
tttgactgga gagaagtga gactcgtgtg ttctcagtg ccatgtgat gatgaagaa 240  
cgagatacca tgttctctgt gacgtgaaa ccccactat atatggccc tgaatatac 300  
aagtactcca atgataaac cattgatgg gaactagaa gggacaagag ggtcaacttgg 360  
attggaggt tctttgcaa ttgtctaat gactgcaat cattgcccc tatctatgt 420  
gaactctccc ttaatacaa ctgtacaggg ctcaatttg ggaaggtgga tgttgaagc 480  
tactatgat ttgtagcgg gtacaaagt agcacatcac cctcaccaa gaactcctt 540  
acctgatcc tgttccaagg tggcaaggag gcaatgggc ggcacagat tgaagaaga 600  
ggacgggtg tctcatggac ctctctgag gagaatgtga tccgagaatt taacttaatt 660  
gagctatacc agcgggcaa gaactatca aaggctggag acaatcccc tgaaggagag 720  
cctgtggtt caacccccc cacagtgtca gatgggaaa acaagaagga taaa 774

15

&lt;210&gt; 137

&lt;211&gt; 330

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

20

&lt;400&gt; 137

atggcgcgg tgttgccaa ggggaaggg ccgcgttca tcaagagggc ggcgtgagg 60  
ggcaacggc cgtctctgga ttatgcgg acctcgtgt cagcgtgtc gggggcagc 120  
gcggcatcc tggcctcac cggcctcac ggtctcatct tctactgct cgcctcgtc 180  
ctgtctccc tgcctcat tctcaaggc ggaaggagt ggaacaaata ttccaatac 240  
cggagacctc tctttacagg aggcctcac gggggcctct tcaactcgt cctgttttg 300  
accttctct acggcatggt gaactctac 330

&lt;210&gt; 138

&lt;211&gt; 273

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

156/177

ctgctccagc aagatctgaa aaaaagaaga agctatggaa acatcatcga ttccagatat 180  
gatgatggaa yggggccaac aggaaacct ccccgagaa tgggtagaat caatcatctg 240  
ctgggcccta gtcacccctc aatgctcgt gga 273

5

<210> 139  
<211> 1032  
<212> DNA  
<213> Homo sapiens

10

<400> 139  
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tttgtgctag acctccacgc agtaagaaga gaactccaga ttgtggaggt gatactgga 180  
agataattt ggcctgattt gaagatact ttctcgagta gtctgcttat ttataattt 240  
aggaattctt aagaagata tggaaagaga aaatttgcct ccttttgcct ggttccctgg 300  
gttttgcag ccttatttga cttccctcct attgaaagta tgaagattt ctttgacatc 360  
acrgacgcta gaaatttgcg ttctgtatgc ctggacactg tgttgcctct gtttgacaa 420  
ttttactcgt ccatccacag agtccaaatg gcaaaatc tgggtccgtt gtccatcaca 480  
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attgtgaca taagtgcact taatgcaggt ctgtgtacg aacgaatat gtccacagtg 600  
cacaagtgct tctgcatcc cagcttgatg gcaaatctt ttctctggac acttgaaacc 660  
atcttctct cttcagaacc caccagcaga gccaaattg ggaatggagc cagcttgac 720  
atccagaagc agcagaagat ggaatgtctg gacggcagc tgaatgtctc tcaatttga 780  
caagggaggg gacagaaga gccagagga gaaatgata attgaaatc tcttttctc 840  
ccttaccgtc agcagacaaa cgtaaatat caggcggctc ggcagctcga gccagcagcg 900  
cccctctag aagttctga ggaacaggtc gcccggtca tggagatgg atttccaga 960  
ggtgagctt tggaaagcct gagaatctca aacaatgac tcaatgtcgc caccacttc 1020  
ctgtgcagc ac 1032

30

<210> 140  
<211> 1284  
<212> DNA  
<213> Homo sapiens

35

&lt;400&gt; 140

156/177

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ctgcaatggt gttcactgct ggcctgaagt ccgaagccac ccggttcccg gggggctgaa 120  
gaaagtctga ccggtacct caagtctc tggcggttc ccgacaggg aatgaacct 180  
acgggtctgg agctgagaga ggaagcgtg taccggcagc actcgcctc ggaagctcgt 240  
gctgggtctc tggtaacgc cgaagggccg gggcgctta accgtctgaa ccgcacacg 300  
aatccacg tgcacacgt ttgggaagc accgtgcaag tctcttgggt ggcctcacc 360  
caagcgcgcg gggcttgcac ctccgaagc aagatcacac tggctatga gaagggggcg 420  
tctggagcgg tcatctttaa ctccccggg acccgcaatg agttcatcc cagtctcac 480  
ccgggtgag tagaatgt tgaatcatg atcggaatc tgaagagac aaaaattctg 540  
caactctacc aagaagagat acaatgaca atgtcatag aatgaaggaa aaaaactggc 600  
ccttgggtga atcactacc aatttttctc gtttctgt ccttttat tatcagggcg 660  
gcaactgtgg gctatttat ctttatct gctcgaagcg taccgaatgc aagaatcaca 720  
agaaggaagc aagggcaat aagcgagat gctaaaaag ctattggag gcttcaacta 780  
cgacacacga acaagggaga caagaaat ggcctgagtg gaagatgtg tctgtgtgc 840  
atgaattgt ataaacaaa tgaattggta cgcactttaa cgtgaacca tatttccat 900  
aagaactgtg ttgaccacg gctgttagaa ccaagacct gcccaatg caaatgtgac 960  
atactaaag ctttggaaat tgaatggat gttgaagatg gataagttc tttaaatc 1020  
cgtgtacca atgaatcac taatgtgc tctcccatg aagaagataa tccgacgag 1080  
aagcatcat ctgtatagc ttcaatagc ggaacagatg aacgcctct ggaagacac 1140  
gtgcaatcaa caaatgaag tctaacgtg gtaaacatg aagaatctc tgttgcaatg 1200  
gaatattc ctcatgtga caaccacac ttggaagag aagaatctc taatcaagag 1260  
actgcgttc gagaatcaa atct 1284

25

<210> 141  
<211> 2050  
<212> DNA  
<213> Homo sapiens

30

<221> CDS  
<222> (122)...(1573)

&lt;400&gt; 141

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tcggaagag ggcgtggc cgggttccg ctgggcac agcttttt ctcaagttgc 120  
a atg aaa gcc ttc cac act ttc tgt gtc gtc ctt ctg gtc ttt ggg 166

157/177

Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly  
 1 5 10 15  
 agt gtc tct gaa gcc aag ttt gat gat ttt gag gat gag gag aac ata 214  
 Ser Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile 30  
 20 25  
 gta gag tat gat gat aat aac gac ttc gct gaa ttt gag gat gtc atg gaa 262  
 Val Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu 45  
 35 40  
 gac tct gtt act gaa tct cct caa cgg gtc ata atc act gaa gat gat 310  
 Asp Ser Val Thr Glu Ser Pro Gln Arg Val Ile Thr Glu Asp Asp 60  
 50 55  
 gaa gat gag acc act gtc gag ttg gaa ggg cag gat gaa aac caa gaa 358  
 Glu Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu 75  
 65 70  
 gga gat ttt gaa gat gca gat acc cag gag gga gat act gag agt gaa 406  
 Gly Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu 95  
 80 85 90  
 cca tat gat gat gaa gaa ttt gaa ggt tat gaa gac aac cca gat act 454  
 Pro Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr 110  
 100 105  
 tct tct agc aac aat aaa gac cca ata acg att gtt gat gtt cct gca 502  
 Ser Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala 125  
 115 120  
 cac ctc cag aac agc tgg gag agt tat tat cta gaa att ttg atg gtc 550  
 His Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val 135  
 130 140  
 act ggt etg ctt gct tat atc atg aat tac atc att ggg aag aat aaa 598  
 Thr Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys 155  
 145 150  
 aac agt cgc ctt gca cag gcc tgg ttt aac act cat agg gag ctt ttg 646  
 Asn Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu 170  
 160 175  
 gag agc aac ttt act tta gtc ggg gat gat gga act aac aac gaa gcc 694  
 Glu Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala 185  
 180 190

35

158/177

aca agc aca gga aag ttg aac cag gag aat gag cac atc tat aac ctg 742  
 Thr Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu 205  
 195 200  
 tgg tgt tct ggt cga gtc tgc gag ggc atg ctt atc cag ctg agg 790  
 5 Trp Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg 220  
 210 215  
 ttc ctc aag aga caa gac tta ctg aat gtc ctg gcc cgg atg atg agg 838  
 Phe Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg 235  
 225 230  
 cca gtc agt gat caa gtc caa ata aaa gta acc atg aat gat gaa gac 886  
 Pro Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp 255  
 240 245  
 atg gat acc tac gta ttt gct gtt ggc aca cgg aaa gcc ttg gtc cga 934  
 Met Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg 265  
 260 270  
 cta cag aaa gag atg cag gat ttg agt gag ttt tgt agt gat aac cct 982  
 Leu Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro 285  
 275 280  
 aag tct gga gca aag tat gga ctg ccg gac tct ttg gcc atc ctg tea 1030  
 Lys Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser 300  
 290 295  
 gag atg gga gaa gtc aca gac gga atg atg gat aca aag atg gtt cac 1078  
 Glu Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His 315  
 305 310  
 ttt ctt aca cac tat gct gac aag att gaa tct gtt cat ttt tca gac 1126  
 Phe Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp 335  
 320 325 330  
 cag ttc tct ggt cca aaa att atg caa gag gaa ggt cag cct tta aag 1174  
 Gln Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys 345  
 340 350  
 cta cct gac act aag agg aca ctg ttg ttt aca ttt aat gtc cct ggc 1222  
 Leu Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly 365  
 355 360  
 tca ggt aac act tac cca aag gat atg gag gca ctg cta ccc ctg atg 1270  
 Ser Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met 385

370 375 380  
 aac atg gtc att tat tct att gat aaa ggc aaa aag ttc cga cta aac 1318  
 aasn met val ile tyr ser ile asp lys ala lys phe arg leu aasn 395  
 385  
 5 aga gaa ggc aaa caa aaa gca gat aag aac cgt gcc cga gta gaa gag 1366  
 arg glu gly lys gln lys ala asp lys aasn arg ala arg val glu glu 415  
 400 405 410 415  
 aac ttc ttg aaa ctg aca cat gtc caa aga cag gaa gca gca cag tct 1414  
 aasn phe leu lys leu thr his val glu arg glu ala ala glu ser 425  
 10 cgg cgg gag gag aaa aaa aga gaa gag aag gag cga atc atg aat gag 1462  
 arg arg glu glu lys lys arg ala glu lys glu arg ile met aasn glu 435 440 445  
 gaa gat cct gag aaa cag cgc agg ctg gag gag gcc gca ttg aag cgt 1510  
 glu asp pro glu lys gln arg leu leu glu ala ala leu arg arg 450 455 460  
 15 gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa atc aaa 1558  
 glu gln lys lys leu glu lys lys gln met lys met lys gln ile lys 465 470 475  
 gtc aaa gcc atg taagcacc ccagagattt gattctgat gccacctgta 1610  
 val lys ala met 480  
 agctctgaat taacagagaa catgaanaac gccagtcgat ttctcaacct taatttcag 1670  
 aagactcttg gccacctgaga aatccttatt taataaccta ctctgtttgg gggttgggt 1730  
 tttaacagaga ttgaagatcc ctggaagggt ctcgtttca agaatcttt ttccaagata 1790  
 atcaaatatt ttgtattatt ttataaagg aatgattcat gaatactggt taggttttaa 1850  
 atattttaa aattatata caaatcatca gtgcttttag taactcagt tttaaganaa 1910  
 taacatgaaa ttataggtta gataaccaga ttgttgcttt ttgtttaac caagagttg 1970  
 aaatgctcat aagaactgac tcataaccaa gattctgcaa ataatgattg gaattgaca 2030  
 ataaacattg ctgtatgctt 2050  
 <210> 142  
 <211> 2746  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> CDS  
 <222> (70)...(1074)  
 <400> 142  
 aaaaactctg ggtgctctcag aacacagag agctcacaga accctgggga gccagctga 60  
 ccgcagcag atg gta gag ttc gcg ccc ttg ttt atg ccg tgg gag cgc 108  
 met val glu phe ala pro leu phe met pro trp glu arg 1  
 1 5 10  
 10 agg ctg cag aca ctt gcc gtc cta cag ttc gtc ttc tcc ttc ttg gca 156  
 arg leu gln thr leu ala val leu gln phe val phe ser phe leu ala 20 25  
 15 ctg gcc gag atc tgc act gtc ggc ttc ata gcc ctg ctg ttc aca aga 204  
 leu ala glu ile cys thr val gly phe ile ala leu leu phe thr arg 35 40 45  
 15 ttc tgg ctg ctg act gcc ctg tat gcg gcc tgg tgg tat ctg gaa cga 252  
 phe trp leu leu thr val leu tyr ala ala trp trp tyr leu asp arg 50 55 60  
 gaa aag caa cgg aag ggg ggc cgg caa atc aag gcc atc aag tgc tgg 300  
 asp lys pro arg gln gly arg his ile gln ala ile arg cys trp 65 70 75  
 20 act ata tgg aag tac atg aag gac tat ttc ccc atc tgg ctg gtc aag 348  
 thr ile trp lys tyr met lys asp tyr phe pro ile ser leu val lys 80 85 90  
 25 act gcc gag ctg gac ccc tct cgg aac tac att gcg ggc ttc caa ccc 396  
 thr ala glu leu asp pro ser arg aasn tyr ile ala gly phe his pro 95 100 105  
 cat gga gtc ctg gaa gtc gga gcc ttc gcc aac ctg tgc act gag agc 444  
 his gly val leu ala val gly ala phe ala aasn leu cys thr glu ser 110 115 120 125  
 30 aca ggc ttc tct tgg atc ttc ccc ggt atc cgc ccc cat ctg atg atg 492  
 thr gly phe ser ser ile phe pro gly ile arg pro his leu met met 130 135 140  
 ctg acc ttg tgg ttc cgg gcc ccc ttc ttc aga gat tac atc atg tct 540  
 leu thr leu trp phe arg ala pro phe phe arg asp tyr ile met ser 150



163/177

<221> CDS  
<222> (32)...(835)  
<400> 143  
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Met Ala Pro Trp Ala Leu Leu  
1 5  
5 atc cct ggg gtc ctc gtc cgg aac ggg cac aac gtc ctc aac tgg gga  
Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly  
10 15 20  
atc aag ctc gtc ctc ttc ctc cag gat aac gag ctc cgg caa tgg gag  
Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Glu Trp Glu  
25 30 35  
gag cag ggg gag ctc ctc ctc ccc ctc acc ttc ctc ctc ctc gtc ctc  
Glu Glu Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Val Leu  
40 45 50 55  
ggc tcc ctc ctc tac ctc gct gtc tca ctc atg gag cct ggc tac  
Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr  
60 65 70  
gtg aat gtc cag ccc cag ccc cag gag gag ctc aaa gag gag cca  
Val Asn Val Glu Pro Glu Pro Glu Glu Leu Lys Glu Glu Thr  
75 80 85  
ggc atg gtc cct cca gcc atc cct ctc cgg cgc tgc aga tac tgc ctc  
Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu  
90 95 100  
gtg ctc cag ccc ctc agg gct cgg cac tgc cgt gag tgc cgc cgt tgc  
Val Leu Glu Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys  
105 110 115  
gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgc gtc gga  
Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly  
120 125 130 135  
gag cgc aac cca cca ttc gtc gtc tac ctc gag cgc ctc gag ctc gtc  
Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Glu Leu Val  
140 145 150  
gtg ctc ctc tgg ggc ctc gca tgg tca gcc ctc cgc ctc ctc  
532

164/177

Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe Phe  
155 160 165  
cag ccc tgg gtc ctc tgg ttc cgg tcc agc ggg ctc ctc ttc gcc aac  
Glu Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr  
170 175 180  
ttc ctc ctc ctc tcc ctc ttc tcc ttc gtc ggc agc ctc ctc ctc  
Phe Leu Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Val  
185 190 195  
tcg cac ctc tac ctc gtc gtc gcc agc aac acc acc acc tgg gaa ttc atc  
Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Trp Glu Phe Ile  
200 205 210 215  
tcc tca cac cgc atc gcc tat ctc cgc cag cgc ccc agc aac ccc ttc  
Ser Ser His Arg Ile Ala Tyr Leu Arg Glu Arg Pro Ser Asn Pro Phe  
220 225 230  
gac cga gcc ctc acc cgc aac ctc gcc ccc ctc ttc tgc gga tgg ccc  
Asp Arg Gly Leu Thr Arg Asn Leu Ala His Phe Cys Gly Trp Pro  
235 240 245  
tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gaa gag ggc agc  
Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Gly Ser  
250 255 260  
agc cca gct gtc taggttgcg ggaagccggg ctaccgcttc gtgcctga  
Ser Pro Ala Val  
265  
aaaccacggg gacgtccccc agctgggtg agcgtcaga gggcctgggg cccctacacc  
tgcaccagcc tcccgagccc cagaacggag ctccagctca gacagatccc tgccttggtg  
ggcagttcgc ccttcacaagg aagaaggga agaaaaggac ctgtgtgttgg ctcaaggcca  
agcagacccc gggctccacc ccagccccc ccaggtctgct gccagtgag acctttacaa  
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930 990 1050 1110 1136  
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165/177

166/177

&lt;222&gt; (13)...(333)

&lt;221&gt; CDS

&lt;222&gt; (111)...(785)

&lt;400&gt; 144

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5 Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro 10

1 aac aea gty ctg agg tac aag ccc ccg ccg agc gaa tgt aac ccg gcc 96

Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala 15

15 ttg gac gac ccg ccg gac tac atg aac ctg ctg ggc atg atc ttc 144

Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe 20

30 agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt gct tgg gtc gct 192

Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala 35

45 gtc tac tgc tcc ttc atc agc ttt gcc aac tct cgg agc tcy gag gac 60

Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp 55

65 aag aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg 288

20 Thr Lys Gln Met Met Ser Phe Met Leu Ser Ile Ser Ala Val Val 70

80 atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg 340

Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp 85

95 tgataccagc ctagaagggt cacatttgg accctgtcta tccactaggc ctgggcttg 390

25 gctgtaaac ctgtgtcctt cagctgccat cctggacttc cctgaatgag gccgtctcg 450

tgccccccagc tggatagagg gaacctggcc ctcttctagg gaacacctta ggcctaccoc 510

tctgcctcc ctctccctgc ctgctgctgg gggagatgct gtccatgttt ctagggtat 570

tcaattgctt tctagtggaa acctgttgtt aataaagttt ttcactcag 619

30

&lt;210&gt; 145

&lt;211&gt; 864

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

5

&lt;400&gt; 145

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ggagccgc ctcgcgatacc ccgcgcgggc gggaccgggc ggcgcgcatc atg acc 116

Met Thr

1

ctg ttt cac ttc ggg aac tgc ttc gct ctt gcc tac ttc ccc tac ttc 164

Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro Tyr Phe 5

10 atc acc tac aag tgc agc ggc ctg tcc gag tac aac gcc ttc tgg aaa 15

Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe Trp Lys 10

20 tgc gtc cag gct gga gtc acc tac ctc ttt gtc caa ctc tgc aag atg 260

Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys Lys Met 25

35 ctg ttc ttg gcc act ttc ttt ccc acc tgg gaa ggc ggc atc tat gac 50

Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Ile Tyr Asp 40

55 ttc att ggg gag ttc atg aag gcc agc gtg gat gtg gca gac ctg ata 65

Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp Leu Ile 60

70 ggt cta aac ctt gtc atg tcc cgg aat gcc ggc aag gga gag tac aag 80

25 Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu Tyr Lys 75

85 atc atg gtt gct gcc ctg ggc tgg gcc act gct gag ctt att atg tcc 95

Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile Met Ser 100

105 cgc tgc att ccc cta tgg gtc gga gcc cgg ggc att gag ttt gac tgg 110

30 Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe Asp Trp 115

120 aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac 125

Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val His Tyr 130

135 35 140 145



167/177

atc gtc ggc tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac 596  
 Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr  
 150 155 160  
 cac acc ttc cgg cca gct gtc ctc ctg atg ttc ctc agt gtc tac 644  
 His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr  
 165 170 175  
 aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc ctg ctg ggc agt 692  
 Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser  
 180 185 190  
 10 tgg gca gct cta ctg ggc cga gaa gtc gta aag ggg ctg ctg ggc ctc 740  
 Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu  
 195 200 205 210  
 agc act ttg ggc ctg tat gtc ggc gtc gtc gtc aac tgc cac tcc tagcttg 790  
 Ser Thr Leu Ala Leu Tyr Val Ala Val Asn Val His Ser  
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 gttattggaa agtc 864  
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 30 ctc gtc tat tgg gtc cgg cga ctc tca cga tgg ctg ggc caa cct tac 99  
 Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr  
 10 15 20 25  
 taa ctc ctg tgg ggc ctg ctc tct gct ggc ttc cta ctc gtc agg aaa 147  
 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

168/177

ctg cgg cgc ctc tgc caa ggt ctg ccc acc caa cgc gaa ggc ggc aac 195  
 Leu Pro Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Asp Gly Asn  
 45 50 55  
 5 cgg tgc gac ttt gac tgg age gaa gtc gag atc ctg atg ttc ctc agt 243  
 Pro Cys Asp Phe Asp Trp Arg Glu Val Ile Leu Met Phe Leu Ser  
 60 65 70  
 ggc att gtc atg atg aag aac cgc aga tcc atg ttc ctg atg aag tgc 291  
 Ala Ile Val Met Met Lys Asn Arg Arg Ser Met Phe Leu Met Thr Cys  
 75 80 85  
 10 aaa ccc ccc cta tat atg ggc cct gag tat atc aag tac ttc aat gat 339  
 Lys Pro Pro Leu Tyr Met Gly Pro Glu Tyr Ile Lys Tyr Phe Asn Asp  
 90 95 100 105  
 aaa acc att gat gag gaa cta gaa cgg gag aag agg gtc act tgg atc 387  
 Lys Thr Ile Asp Glu Leu Leu Glu Arg Asp Lys Arg Val Thr Trp Ile  
 110 115 120  
 15 gtc gag ttc ttt gac aat tgg tct aat gac tgc cca tta ttt ggc cct 435  
 Val Glu Phe Phe Ala Asn Trp Ser Asn Asp Cys Gln Ser Phe Ala Pro  
 125 130 135  
 atc tat gct gac ctc tcc ctt aaa tac aac tgt aca ggg cta aat ttt 483  
 Ile Tyr Ala Asp Leu Ser Leu Lys Tyr Asn Cys Thr Gly Leu Asn Phe  
 140 145 150  
 ggg aag gtc gat gtc gga cgc tat act gat gtc agt aag cgg tac aaa 531  
 Gly Lys Val Asp Val Gly Arg Tyr Thr Asp Val Ser Thr Arg Tyr Lys  
 155 160 165  
 25 gtc ago aca tca ccc ctc acc aag caa ctc cct acc ctg atc ctg ttc 579  
 Val Ser Thr Ser Pro Leu Thr Lys Gln Leu Pro Thr Leu Ile Leu Phe  
 170 175 180 185  
 caa ggt ggc aag gag gaa atg cgg cgg cca cag att gac aag aaa gga 627  
 Gln Gly Gly Lys Glu Ala Met Arg Arg Pro Gln Ile Asp Lys Lys Gly  
 190 195 200  
 30 cgg gct gtc tca tgg acc ttc tct gag gag aat gtc atc cga gaa ttt 675  
 Arg Ala Val Ser Trp Thr Phe Ser Glu Glu Asn Val Ile Arg Glu Phe  
 205 210 215  
 35 aac tta aat gag cta tac cag cgg ggc aag aag aaa cta tca aag gct gga 723

169/177

170/177

5	Asn Leu Asn Glu Leu Tyr Gln Arg Ala Lys Lys Leu Ser Lys Ala Gly 220 225 230 gac aat atc cct gag gag cag cct-gtg get tca acc ccc acc aca gtg 771 Asp Asn Ile Pro Glu Glu Gln Pro Val Ala Ser Thr Pro Thr Thr Val 235 240 245 tca gat ggg gaa aac aag aag gat aaa taagatcctc ac 810 Ser Asp Gly Glu Asn Lys Lys Asp Lys 250 255 tttggcagtg cttcctctcc tgcctaatcc aggtctcttc cataaccaca agcctgagge 870 10 tgcagcttt tatttatgtt ttccctttgg ctgtgactgg gtggggcagc atgcagcttc 930 tgattttaaa gaggcataceta ggggaattgce aggcacccta cagggaaggcc tgcctatgctg 990 tgcccaactg ttctactgga gcaagaaga gatctcatag gacggggggg gaaatggttt 1050 ccctccagc tggggcagtg gtgttaactg cttatcagct attcagcact ctcctatggtt 1110 tctccatgaa actctgtggt ttcatccttc cttcttagtt gacctgcaca gcttggttag 1170 acctagatt aacctaaagg taagatgctg gggatagaa cgttaagaat ttcccccac 1230 ggactcttgc ttccctnagc cctcttggt tegttaag tctctatnag aagtaaga 1290 ctaactttgt cgtctagctc aaggagaac ctttaaccac aagtttttta tcaatgaaga 1350 caatattgaa caaccacctc ttttggggg attgagaagg ggtgaataga gctttgagac 1410 tttctttgt gtggtaggac ttgaaggaga aatccctgg acttccacta accctctgac 1470 atactcccca caccacgtg atggctttcc gtaataanaa gattgggatt tcccttt 1527	218 266 314 362 410 458 500 560 620 659
25	<210> 147 <211> 659 <212> DNA <213> Homo sapience <220> <221> CDS <222> (138)...(470)	
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35	<400> 148 agagggagat acagaaaccg acagggggcca ggcgcctggt ggtcccgaa gggggaagtg 60	560 620 659

171/177

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Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser  
1 5 10  
cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata 157  
Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile  
15 20 25 30  
gct gag ttt gtc gtc ttt ttc aac act ctg ctt cag caa gat gtc 205  
Ala Gln Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Asp Val  
35 40 45  
10 aaa aaa aga aga agc tat gga aac tca tct gat tcc aga tat gat 253  
Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp  
50 55 60  
gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat 301  
Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn  
65 70 75  
15 cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tgaagaagt 350  
His Leu Arg Gly Pro Ser Pro Pro Met Ala Gly Gly  
80 85 90  
20 aatgtctgc tctaaagac agacaacgg ncatgagat tcatagaga agaaacat 410  
caagaagtgg aaggtgac atgaltgaga gtagatgat ggtatgct aaaaagac 470  
tgctctgtt cctcaagat gaatgagtc atgctggaa ttcctctgc aggaactg 530  
cctgaatgaa atgaatgcc ataatgag atgttgct catcaactc ttrataagt 590  
tataaaga ttaatatgt ttaataagt aatatctt aggtgaga atgactcct 650  
catcttata ttaagaaa agaatctga agaaacaaa taaagctg tttattagc 710  
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35 <400> 149  
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172/177

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Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser  
1 5 10 15  
aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc ctc 151  
Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu  
20 25 30  
ctc ctg cct ccc tgc cag aag ctc ttt gtc tat gac ctt cac gca gtc 199  
Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val  
35 40 45  
10 aag aac gac ttc cag att tgg agt ttg ata tgt gga aga ata atc tgc 247  
Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys  
50 55 60  
ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttt 295  
Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe  
65 70 75 80  
15 agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca too ttt ttg 343  
Arg Ile Phe Gln Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu  
85 90 95  
20 ctg ggt tcc tgg gtc ttg tca gcc tta ttt gac ttt ctc ctc att gaa 391  
Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Gln  
100 105 110  
gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg cct tct 439  
Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser  
115 120 125  
25 gga ttc ctg gca cct gtc ttt gct ctg ttt gta cca ttt tac tgc tcc 487  
Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser  
130 135 140  
ata cca aga gtc cca gtc gca cca att ctg ggt ccg ttg tcc atc aca 535  
Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr  
145 150 155 160  
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Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly  
165 170 175  
35 tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc 631  
Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys

173/177

174/177

5 tac gac agc aaa atg ttc cag atg cat cag gtc etc tgc atc ccc agc 679  
 Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser 205  
 195  
 5 tgg atg gca aaa ttc ttt ttt tgg aca ctt gaa ccc atc ttc tct tct 727  
 Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser 220  
 210  
 10 tea gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac 775  
 Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp 235  
 225 atc cag aga cag cag aga atg gag ctg gac cgg cag ctg atg ttc 240  
 Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe 255  
 245  
 15 tct cag ttt gca caa ggg agc cga cag aga cag cag gga gga atg 871  
 Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Met 270  
 260  
 20 etc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta 919  
 Ile Asn Trp Asn Arg Leu Phe Pro Leu Arg Gln Arg Gln Asn Val 285  
 275  
 20 aac tat cag ggc ggt cgg cag tct gag cca gca ggc ccc cct cta gaa 967  
 Asn Tyr Gln Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu 300  
 290  
 25 gtt tct gag gaa cag gtc gcc cgg etc atg gag atg gga ttt tcc aga 1015  
 Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg 315  
 305 ggt gat gct ttg gaa gcc ctg aga gct tca aac aat gac etc aat gtc 1063  
 Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val 335  
 325  
 30 gcc acc aac ttc ctg ctg cag cac tgatgtccc aggcacacac tgg 1110  
 Ala Thr Asn Phe Leu Leu Gln His 340  
 35 gaccggaccg gcagccaggt gacagtgcgt ggtcccccacc atcagatcag cccgggacc 1170  
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 caaccgcag actgtgccc ttttgtgtg gagataagtt tgcattaca ttgcatgta 1290  
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gaatgttt aaatgcatt aaatggag attctggag gaagtgaat ggcactccag 1410  
 atggggnaat gctgtacccc tctactgta acatgcatc tootgcgtcg tgatggggag 1470  
 aggttaatgt tacttcaaaa aggaatgct agatcctct toatggaatt ttttagttac 1530  
 tgtttttct ctcaaatctg ttttgaatc tctggggagt gaggggagaaa caggggagctg 1590  
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 ctcaaggctt ggggtctcaa cctgtggga caggaggcag ggcagaatgt ggaaggcagg 2070  
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 caagtgaact ctggcaatgt gcaactgta tgtctgcaa aatgagcaac gatgataca 2182  
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 cctggcgc acctgctcaa gaccaggctc ctgcacagc ctaggagggc gcgtgcagg 180  
 ggcgtaggg aactggagc cgcgcgcgc atg ggg ccg cct ggg gcc 231  
 Met Gly Pro Pro Gly Ala  
 30 ggg gtc tcc tgc cgc ggt ggc tgc ggc ttt tcc aga ttg ctg gca tgg 279  
 Gly Val Ser Cys Arg Gly Cys Gly Phe Ser Arg Leu Leu Ala Trp  
 10 15 20  
 tgc ttc ctg ctg gcc atg cag cag gca ccc ggt tcc cgg ggg gct 327  
 Cys Phe Leu Leu Ala Leu Ser Pro Gln Ala Pro Gly Ser Arg Gly Ala

176/177

25 30 35  
gaa gaa gtc tgg acc ggc tac ctc aac gtc tcc tgg cgg gtc ccc cac 375  
Glu Ala Val Trp Thr Ala Tyr Leu Asn Val Ser Trp Arg Val Pro His  
40 45 50 55  
aac gga gtc aac cgt aac gtc tgg ggc ctc agc gaa gaa ggc gtc tac 423  
Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Gly Val Tyr  
60 65 70  
ggc cag gac tcc ccc gtc ggc cct gtc gct ggg gtc gtc gtc ccc 471  
Gly Glu Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro  
75 80 85  
gac ggg ccc ggg ggc ctc aac ggc tgc aac ccc ccc aac aac ttc aac 519  
Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr  
90 95 100  
gtc ccc aac gtc tgg gga agc aac gtc gaa gtc tcc tgg ttc ggc ctc 567  
Val Pro Thr Val Trp Gly Ser Thr Val Glu Val Ser Trp Leu Ala Leu  
105 110 115  
aac caa cgc ggc ggg ggc tgc acc ttc gaa gac aag aac ctc gtc gct 615  
Ile Glu Arg Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala  
120 125 130 135  
cat gaa aga ggg ggc tcc gga ggc gtc aac ttc aac ttc ccc ggg aac 663  
Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr  
140 145 150  
cgc aac gaa gtc aac ccc atg tcc ccc ccc ggc ggc gtc aac aac gtc 711  
Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val  
155 160 165  
gaa atc atg atc ggc aac ctc aaa ggc aca aaa aac ctc gaa tcc att 759  
Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Glu Ser Ile  
170 175 180  
aaa aga ggc ata caa gtc aca atg gtc ata gaa gtc ggg aaa aac cat 807  
Glu Arg Gly Ile Glu Val Thr Met Val Ile Glu Val Gly Lys Lys His  
185 190 195  
ggc cct tgg gtc aac ccc tcc att ttc ttc gtc tcc gtc tcc ttc 855  
Gly Pro Trp Val Asn His Tyr Ser Ile Phe Phe Val Ser Val Ser Phe  
200 205 210 215  
ttt att att aac ggc gaa aac gtc ggc tcc ttc att ttc tcc tcc gct 903

176/177

Phe Ile Ile Thr Ala Ala Thr Val Gly Tyr Phe Ile Phe Tyr Ser Ala  
220 225 230  
cga agc cta cgg aac gaa agc ccc aac agc aag aag aag aac tta 951  
Arg Arg Leu Arg Asn Ala Arg Ala Glu Ser Arg Lys Glu Arg Glu Leu  
235 240 245  
aag gaa gac gtc aac aac gct att gga aag ctc aac cta ccc aac ctc 999  
Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Leu Arg Thr Leu  
250 255 260  
aaa caa gga gac aag gaa att ggc ccc gac gga gac agt tgc gtc gtc 1047  
Lys Glu Gly Asp Lys Glu Ile Gly Pro Asp Gly Asp Ser Cys Ala Val  
265 270 275  
tgc att gaa ttc tat aac cca aac gac ttc gtc gtc aac tta aac tgc 1095  
Cys Ile Glu Leu Tyr Lys Pro Asn Asp Leu Val Arg Ile Leu Thr Cys  
280 285 290 295  
aac cat att ttc cat aag aca tgc gtc gac cca tgg ctc tta gaa ccc 1143  
Asn His Ile Phe His Lys Thr Cys Val Asp Pro Trp Leu Glu His  
300 305 310  
aag act tgc ccc atg tgc aac tgc gac ata ctc aac gct ttc gga att 1191  
Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile  
315 320 325  
gag gtc gat gtc gaa gat gga tca gtc tcc tta caa gtc ccc gta tcc 1239  
Glu Val Asp Val Glu Asp Gly Ser Val Ser Leu Glu Val Pro Val Ser  
330 335 340  
aat gaa ata tcc aat agt ggc tcc tcc cat gaa gaa gat aac cgc aag 1287  
Asn Glu Ile Ser Asn Ser Ala Ser Ser His Glu Glu Asp Asn Arg Ser  
345 350 355  
gag acc gaa tca tcc gga tcc gac tca gta cag gga aca gat gaa ccc 1335  
Glu Thr Ala Ser Ser Gly Tyr Ala Ser Val Glu Gly Thr Asp Glu Pro  
360 365 370 375  
cct ctc gag gaa ccc gtc cag tca aca aac aac agt cta cag ctc gta 1383  
Pro Leu Glu Glu His Val Glu Ser Thr Asn Glu Ser Leu Glu Leu Val  
380 385 390  
aac cat gaa gaa aac tcc gtc gaa gtc gat att ccc cat gtc gac 1431  
Asn His Glu Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp  
395 400 405

177/177

1479	aac cca acc ttt gaa gaa gac gaa aet cct aat caa gag act gct gtt	420	1530
	Aan Pro Thr Phe Glu Glu Asp Glu Thr Pro Asn Gln Glu Thr Ala Val	415	
	cga gaa att aaa tct taaaatctgt gtaaatagaa aacttgaacc attagt	410	
	Arg Glu Ile Lys Ser	425	
1590	aataacagaa ctgcgaacta gggcctagt tctattaata aattggataa atttaataa		1650
1650	atcagagtg taactgaagt gtcacagatga ctaactatt gctatagtta aatgcttaa		1710
1710	aataatcaac ctgttaact ttttcacaa aatcalkata atattttta tagcnaagt		1770
1770	tactctagt agtgataaca acatttttag acattcaaaa ctgtcttcaa gaagtcaagt		1830
1830	ttttcaatta taacantttt ctataaaaa catgttgctt taaaatgty gagtagctgt		1890
1890	aatcaactta ttttcagata gtaacttaat gaanaact actctcttag cttyggctac		1950
1950	atgtgtcagg gttttttctc aggtgttat attgaacttg aattgtaaty taanaagcaa		2010
2010	tgcaaaccta ggcgagtaact tcttgaatg tctctttaag ctgcttttag ttaatagaaa		2070
2070	agattnaagc aanaattctta tttttactt tctctattt taaaattagg ctgaatgtac		2130
2130	ttaactgat ttgcacaaca tagttatcaa gagatattg acttaattga ttggtatatt		2190
2190	agtgacatca acttgacaca agattagaca aanaattctc tacaanaata ctgtgaact		2250
2250	atttctaaa ctgtggggat ttttcanaag ctongtatat gaatcatcat actgtttgaa		2310
2310	attgctaaty acagagttag taacactaat attggtcatt gatcttgctt catgaattag		2370
2370	tctacagaaa aaaaatgttc tgtaaaatta gctctgtgaa aatgttttcc aaaaatgtt		2430
2430	actttgaaaa ttgagtttat gtttgaccta aatgggctaa aattatatta gataaactaa		2490
2490	aattctgoc gttgaactat aaattttgt aatgcatttt cctggtgttt gnaaagaag		2550
2550	ggggggagaa, ttccaggtgc cttaactaaa agttgaagc ttcatcacc aagttaaat		2610
2610	agagctatt aaaaatgcac tttaattgta cctctgtggy cttttgtttt agaatttgt		2670
2670	tcaaatata gcagaattta ggcnaaaata aaaaagacat gtaattttgt ttctgtaaty		2730
2730	gatgaaccaa ttgcattctt gtacactgat ttgaatgct gtaaatatgt ccccaattgt		2773
2773	attgattctc tttaaatata aaatgttaat aaatatcc aat		